## 10/565058

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<110> Hardie, David Grahame Alessi, Dario Boudeau, Jerome

<120> Methods For Use of An LKb1/Strad7M025 Complex

<130> 002.00270

The fee with 8

<150> PCT/GB2004/003096

<151> 2004-07-16

<150> GB 0316725.1

<151> 2003-07-17

<150> GB 0330078.7

<151> 2003-12-20

<160> 158

<170> PatentIn version 3.1

<210> 1

<211> 550 .

<212> PRT

<213> Homo sapiens

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His Tyr Ile Leu Gly Asp Thr Leu Gly Val Gly Thr Phe Gly Lys Val 20 25 30

Lys Val Gly Lys His Glu Leu Thr Gly His Lys Val Ala Val Lys Ile 35 40 45

Leu Asn Arg Gln Lys Ile Arg Ser Leu Asp Val Val Gly Lys Ile Arg 50 55 60

Arg Glu Ile Gln Asn Leu Lys Leu Phe Arg His Pro His Ile Ile Lys 65 70 75 80

Leu Tyr Gln Val Ile Ser Thr Pro Ser Asp Ile Phe Met Val Met Glu 85 90 95

Tyr Val Ser Gly Gly Glu Leu Phe Asp Tyr Ile Cys Lys Asn Gly Arg 100 105 110

Leu Asp Glu Lys Glu Ser Arg Arg Leu Phe Gln Gln Ile Leu Ser Gly 115 120 125

Val Asp Tyr Cys His Arg His Met Val Val His Arg Asp Leu Lys Pro 130 135 140

Glu Asn Val Leu Leu Asp Ala His Met Asn Ala Lys Ile Ala Asp Phe 145 150 155 160

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- Gly Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys 165 170 175
- Gly Ser Pro Asn Tyr Ala Ala Pro Glu Val Ile Ser Gly Arg Leu Tyr 180 185 190
- Ala Gly Pro Glu Val Asp Ile Trp Ser Ser Gly Val Ile Leu Tyr Ala 195 200 205
- Leu Leu Cys Gly Thr Leu Pro Phe Asp Asp Asp His Val Pro Thr Leu 210 215 220
- Phe Lys Lys Ile Cys Asp Gly Ile Phe Tyr Thr Pro Gln Tyr Leu Asn 225 230 235 240
- Pro Ser Val Ile Ser Leu Leu Lys His Met Leu Gln Val Asp Pro Met 245 250 255
- Lys Arg Ala Thr Ile Lys Asp Ile Arg Glu His Glu Trp Phe Lys Glu 260 265 270
- Asp Leu Pro Lys Tyr Leu Phe Pro Glu Asp Pro Ser Tyr Ser Ser Thr 275 280 285
- Met Ile Asp Asp Glu Ala Leu Lys Glu Val Cys Glu Lys Phe Glu Cys 290 295 300
- Ser Glu Glu Glu Val Leu Ser Cys Leu Tyr Asn Arg Asn His Gln Asp 305 310 315 320
- Pro Leu Ala Val Ala Tyr His Leu Ile Ile Asp Asn Arg Arg Ile Met  $325 \hspace{1.5cm} 330 \hspace{1.5cm} 335$
- Asn Glu Ala Lys Asp Phe Tyr Leu Ala Thr Ser Pro Pro Asp Ser Phe 340 345 350
- Leu Asp Asp His His Leu Thr Arg Pro His Pro Glu Arg Val Pro Phe 355 360 365
- Leu Val Ala Glu Thr Pro Arg Ala Arg His Thr Leu Asp Glu Leu Asn  $370 \hspace{1.5cm} 375 \hspace{1.5cm} 380$

Pro Gln Lys Ser Lys His Gln Gly Val Arg Lys Ala Lys Trp His Leu 385 390 395 400

Gly Ile Arg Ser Gln Ser Arg Pro Asn Asp Ile Met Ala Glu Val Cys  $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$ 

Arg Ala Ile Lys Gln Leu Asp Tyr Glu Trp Lys Val Val Asn Pro Tyr 420 425 430 .

Tyr Leu Arg Val Arg Arg Lys Asn Pro Val Thr Ser Thr Tyr Ser Lys 435 440 445

Met Ser Leu Gln Leu Tyr Gln Val Asp Ser Arg Thr Tyr Leu Leu Asp 450 460

Phe Arg Ser Ile Asp Asp Glu Ile Thr Glu Ala Lys Ser Gly Thr Ala 465 470 475 480

Thr Pro Gln Arg Ser Gly Ser Val Ser Asn Tyr Arg Ser Cys Gln Arg 485 490 495

Ser Asp Ser Asp Ala Glu Ala Gln Gly Lys Ser Ser Glu Val Ser Leu 500 505 510

Thr Ser Ser Val Thr Ser Leu Asp Ser Ser Pro Val Asp Leu Thr Pro 515 520 525

Arg Pro Gly Ser His Thr Ile Glu Phe Phe Glu Met Cys Ala Asn Leu 530 540

Ile Lys Ile Leu Ala Gln 545 550

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<211> 550

<212> PRT

<213> Homo sapiens

<400> 2

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His Tyr Ile Leu Gly Asp Thr Leu Gly Val Gly Thr Phe Gly Lys Val

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Leu Asn Arg Gln Lys Ile Arg Ser Leu Asp Val Val Gly Lys Ile Arg 50 55 60

Arg Glu Ile Gln Asn Leu Lys Leu Phe Arg His Pro His Ile Ile Lys 65 70 75 80

Leu Tyr Gln Val Ile Ser Thr Pro Ser Asp Ile Phe Met Val Met Glu 85 90 95

Tyr Val Ser Gly Gly Glu Leu Phe Asp Tyr Ile Cys Lys Asn Gly Arg 100 105 110

Leu Asp Glu Lys Glu Ser Arg Arg Leu Phe Gln Gln Ile Leu Ser Gly 115 120 125

Val Asp Tyr Cys His Arg His Met Val Val His Arg Asp Leu Lys Pro 130 135 140

Glu Asn Val Leu Leu Asp Ala His Met Asn Ala Lys Ile Ala Asp Phe 145 150 155 160

Gly Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys 165 170 175

Gly Ser Pro Asn Tyr Ala Ala Pro Glu Val Ile Ser Gly Arg Leu Tyr 180 185 190

Ala Gly Pro Glu Val Asp Ile Trp Ser Ser Gly Val Ile Leu Tyr Ala 195 200 205

Leu Leu Cys Gly Thr Leu Pro Phe Asp Asp His Val Pro Thr Leu 210 215 220

Phe Lys Lys Ile Cys Asp Gly Ile Phe Tyr Thr Pro Gln Tyr Leu Asn 225 230 235 240

Pro Ser Val Ile Ser Leu Leu Lys His Met Leu Gln Val Asp Pro Met 245 250 255

Lys Arg Ala Ser Ile Lys Asp Ile Arg Glu His Glu Trp Phe Lys Gln  $260 \hspace{1cm} 265 \hspace{1cm} 270 \hspace{1cm}$ 

Asp Leu Pro Lys Tyr Leu Phe Pro Glu Asp Pro Ser Tyr Ser Ser Thr 275 280 285

Met Ile Asp Asp Glu Ala Leu Lys Glu Val Cys Glu Lys Phe Glu Cys 290 295 300

Ser Glu Glu Glu Val Leu Ser Cys Leu Tyr Asn Arg Asn His Gln Asp 305 310 315 320

Pro Leu Ala Val Ala Tyr His Leu Ile Ile Asp Asn Arg Arg Ile Met 325 330 335

Asn Glu Ala Lys Asp Phe Tyr Leu Ala Thr Ser Pro Pro Asp Ser Phe 340 345 350

Leu Asp Asp His His Leu Thr Arg Pro His Pro Glu Arg Val Pro Phe 355 360 365

Leu Val Ala Glu Thr Pro Arg Ala Arg His Thr Leu Asp Glu Leu Asn  $370 \hspace{1.5cm} 375 \hspace{1.5cm} 380$ 

Pro Gln Lys Ser Lys His Gln Gly Val Arg Lys Ala Lys Trp His Leu 385 390 395 400

Gly Ile Arg Ser Gln Ser Arg Pro Asn Asp Ile Met Ala Glu Val Cys  $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$ 

Arg Ala Ile Lys Gln Leu Asp Tyr Glu Trp Lys Val Val Asn Pro Tyr 420 425 430

Tyr Leu Arg Val Arg Arg Lys Asn Pro Val Thr Ser Thr Tyr Ser Lys 435 440 445

Met Ser Leu Gln Leu Tyr Gln Val Asp Ser Arg Thr Tyr Leu Leu Asp 450 460

Phe Arg Ser Ile Asp Asp Glu Ile Thr Glu Ala Lys Ser Gly Thr Ala 465 470 475 480

Thr Pro Gln Arg Ser Gly Ser Val Ser Asn Tyr Arg Ser Cys Gln Arg 485 490 495

Ser Asp Ser Asp Ala Glu Ala Gln Gly Lys Ser Ser Glu Val Ser Leu 500 505 510

Thr Ser Ser Val Thr Ser Leu Asp Ser Ser Pro Val Asp Leu Thr Pro 515 520 525

Arg Pro Gly Ser His Thr Ile Glu Phe Phe Glu Met Cys Ala Asn Leu 530 540

Ile Lys Ile Leu Ala Gln 545 550

<210> 3

<211> 550

<212> PRT

<213> Homo sapiens

<400> 3

Met Ala Thr Ala Glu Lys Gln Lys His Asp Gly Arg Val Lys Ile Gly
1 5 10 15

His Tyr Ile Leu Gly Asp Thr Leu Gly Val Gly Thr Phe Gly Lys Val  $20 \\ 25 \\ 30$ 

Lys Val Gly Lys His Glu Leu Thr Gly His Lys Val Ala Val Lys Ile 35 40 45

Leu Asn Arg Gln Lys Ile Arg Ser Leu Asp Val Val Gly Lys Ile Arg 50 55 60

Arg Glu Ile Gln Asn Leu Lys Leu Phe Arg His Pro His Ile Ile Lys 65 70 75 80

Leu Tyr Gln Val Ile Ser Thr Pro Ser Asp Ile Phe Met Val Met Glu 85 90 95

Tyr Val Ser Gly Glu Leu Phe Asp Tyr Ile Cys Lys Asn Gly Arg 100 105 110

Leu Asp Glu Lys Glu Ser Arg Arg Leu Phe Gln Gln Ile Leu Ser Gly

115 120 125

Val	Asp 130	Tyr	Cys	His	Arg	His 135	Met	Val	Val	His	Arg 140	Asp	Leu	Lys	Pro
Glu 145	Asn	Val	Leu	Leu	Asp 150	Ala	His	Met	Asn	Ala 155	Lys	Ile	Ala	Asp	Phe 160
Gly	Leu	Ser	Asn	Met 165	Met	Ser	Asp	Gly	Glu 170	Phe	Leu	Arg	Thr	Ser 175	Cys
Gly	Ser	Pro	Asn 180	Tyr	Ala	Ala	Pro	Glu 185	Val	Ile	Ser	Gly	Arg 190	Leu	Туз
Ala	Gly	Pro 195	Glu	Val	Asp	Ile	Trp 200	Ser	Ser	Gly	Val	Ile 205	Leu	Tyr	Ala
Leu	Leu 210	Cys	Gly	Thr	Leu	Pro 215	Phe	Asp	Asp	Asp	His 220	Val	Pro	Thr	Le
Phe 225	Lys	Lys	Ile	Cys	Asp 230	Gly	Ile	Phe	Tyr	Thr 235	Pro	Gln	Tyr	Leu	Asr 240
Pro	Ser	Val	Ile	Ser 245	Leu	Leu	Lys	His	Met 250	Leu	Gln	Val	Asp	Pro 255	Met
Lys	Arg	Ala	Ser 260	Ile	Lys	Asp	Ile	Arg 265	Glu	His	Glu	Trp	Phe 270	Lys	Glr
Asp	Leu	Pro 275	Lys	Tyr	Leu	Phe	Pro 280	Glu	Asp	Pro	Ser	Tyr 285	Ser	Ser	Thi
Met	Ile 290	Asp	Asp	Glu	Ala	Leu 295	Lys	Glu	Val	Cys	Glu 300	Lys	Phe	Glu	Cys
Ser 305	Glu	Glu	Glu	Val	Leu 310	Ser	Cys	Leu	Tyr	Asn 315	Arg	Asn	His	Gln	Asp 320
Pro	Leu	Ala	Val	Ala 325	Tyr	His	Leu	Ile	Ile 330	Asp	Asn	Arg	Arg	Ile 335	Met
Asn	Glu	Ala	Lys 340	Asp	Phe	Tyr	Leu	Ala 345	Thr	Ser	Pro	Pro	Asp 350	Ser	Ph€

Leu Asp Asp His His Leu Thr Arg Pro His Pro Glu Arg Val Pro Phe 355 360 365

Leu Val Ala Glu Thr Pro Arg Ala Arg His Thr Leu Asp Glu Leu Asn 370 375 380

Pro Gln Lys Ser Lys His Gln Gly Val Arg Lys Ala Lys Trp His Leu 385 390 395 400

Gly Ile Arg Ser Gln Ser Arg Pro Asn Asp Ile Met Ala Glu Val Cys 405 410 415

Arg Ala Ile Lys Gln Leu Asp Tyr Glu Trp Lys Val Val Asn Pro Tyr 420 425 430

Tyr Leu Arg Val Arg Arg Lys Asn Pro Val Thr Ser Thr Tyr Ser Lys 435 440 445

Met Ser Leu Gln Leu Tyr Gln Val Asp Ser Arg Thr Tyr Leu Leu Asp 450 460

Phe Arg Ser Ile Asp Asp Glu Ile Thr Glu Ala Lys Ser Gly Thr Ala 465 470 475 480

Thr Pro Gln Arg Ser Gly Ser Val Ser Asn Tyr Arg Ser Cys Gln Arg 485 490 495

Ser Asp Ser Asp Ala Glu Ala Gln Gly Lys Ser Ser Glu Val Ser Leu 500 505 . 510

Thr Ser Ser Val Thr Ser Leu Asp Ser Ser Pro Val Asp Leu Thr Pro 515 520 525

Arg Pro Gly Ser His Thr Ile Glu Phe Phe Glu Met Cys Ala Asn Leu 530 540

Ile Lys Ile Leu Ala Gln 545 550

<210> 4 <211> 520 <212> PRT <213> Homo sapiens

<400> 4

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Ile Gln Asn Leu Lys Leu Phe Arg His Pro His Ile Ile Lys Leu Tyr 35 40 45

Gln Val Ile Ser Thr Pro Thr Asp Phe Phe Met Val Met Glu Tyr Val 50 55 60

Ser Gly Gly Glu Leu Phe Asp Tyr Ile Cys Lys His Gly Arg Val Glu 65 70 75 80

Glu Met Glu Ala Arg Arg Leu Phe Gln Gln Ile Leu Ser Ala Val Asp 85 90 95

Tyr Cys His Arg His Met Val Val His Arg Asp Leu Lys Pro Glu Asn 100 . 105 110

Val Leu Leu Asp Ala His Met Asn Ala Lys Ile Ala Asp Phe Gly Leu
115 120 125

Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys Gly Ser 130 135 140

Pro Asn Tyr Ala Ala Pro Glu Val Ile Ser Gly Arg Leu Tyr Ala Gly 145 150 155 160

Pro Glu Val Asp Ile Trp Ser Cys Gly Val Ile Leu Tyr Ala Leu Leu 165 170 175

Cys Gly Thr Leu Pro Phe Asp Asp Glu His Val Pro Thr Leu Phe Lys 180 185 190

Lys Ile Arg Gly Gly Val Phe Tyr Ile Pro Glu Tyr Leu Asn Arg Ser 195 200 205

Val Ala Thr Leu Leu Met His Met Leu Gln Val Asp Pro Leu Lys Arg

Ala Thr Ile Lys Asp Ile Arg Glu His Glu Trp Phe Lys Gln Asp Leu 225 230 235 240

Pro Ser Tyr Leu Phe Pro Glu Asp Pro Ser Tyr Asp Ala Asn Val Ile 245 250 255

Asp Asp Glu Ala Val Lys Glu Val Cys Glu Lys Phe Glu Cys Thr Glu 260 265 270

Ser Glu Val Met Asn Ser Leu Tyr Ser Gly Asp Pro Gln Asp Gln Leu 275 280 285

Ala Val Ala Tyr His Leu Ile Ile Asp Asn Arg Arg Ile Met Asn Gln 290 295 300

Ala Ser Glu Phe Tyr Leu Ala Ser Ser Pro Pro Ser Gly Ser Phe Met 305 310 315

Asp Asp Ser Ala Met His Ile Pro Pro Gly Leu Lys Pro His Pro Glu 325 330 335

Arg Met Pro Pro Leu Ile Ala Asp Ser Pro Lys Ala Arg Cys Pro Leu 340 345 350

Asp Ala Leu Asn Thr Thr Lys Pro Lys Ser Leu Ala Val Lys Lys Ala 355 360 365

Lys Trp His Leu Gly Ile Arg Ser Gln Ser Lys Pro Tyr Asp Ile Met  $370 \hspace{1.5cm} 375 \hspace{1.5cm} 380$ 

Ala Glu Val Tyr Arg Ala Met Lys Gln Leu Asp Phe Glu Trp Lys Val 385 390 395 400

Val Asn Ala Tyr His Leu Arg Val Arg Lys Asn Pro Val Thr Gly
405 410 415

Asn Tyr Val Lys Met Ser Leu Gln Leu Tyr Leu Val Asp Asn Arg Ser 420 425 430

Tyr Leu Leu Asp Phe Lys Ser Ile Asp Asp Glu Val Val Glu Gln Arg 435 440 445

Ser Gly Ser Ser Thr Pro Gln Arg Ser Cys Ser Ala Ala Gly Leu His 450 . 455 . 460

Arg Pro Arg Ser Ser Phe Asp Ser Thr Thr Ala Glu Ser His Ser Leu 465 470 475 480

Ser Gly Ser Leu Thr Gly Ser Leu Thr Gly Ser Thr Leu Ser Ser Val $485 \hspace{1.5cm} 490 \hspace{1.5cm} 495$ 

Ser Pro Arg Leu Gly Ser His Thr Met Asp Phe Phe Glu Met Cys Ala 500 505 510

Ser Leu Ile Thr Thr Leu Ala Arg 515 520

<210> 5

<211> 552

<212> PRT

<213> Homo sapiens

<400> 5

Met Ala Glu Lys Gln Lys His Asp Gly Arg Val Lys Ile Gly His Tyr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Val Leu Gly Asp Thr Leu Gly Val Gly Thr Phe Gly Lys Val Lys Ile 20 25 30

Gly Glu His Gln Leu Thr Gly His Lys Val Ala Val Lys Ile Leu Asn  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Arg Gln Lys Ile Arg Ser Leu Asp Val Val Gly Lys Ile Lys Arg Glu 50 55 60

Ile Gln Asn Leu Lys Leu Phe Arg His Pro His Ile Ile Lys Leu Tyr 75 75 80

Gln Val Ile Ser Thr Pro Thr Asp Phe Phe Met Val Met Glu Tyr Val 85 90 95

Ser Gly Glu Leu Phe Asp Tyr Ile Cys Lys His Gly Arg Val Glu 100 105 110

Glu Met Glu Ala Arg Arg Leu Phe Gln Gln Ile Leu Ser Ala Val Asp 115 120 125

Tyr Cys His Arg His Met Val Val His Arg Asp Leu Lys Pro Glu Asn 130 140

Val Leu Leu Asp Ala His Met Asn Ala Lys Ile Ala Asp Phe Gly Leu 145 150 155 160

Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys Gly Ser 165 170 175

Pro Asn Tyr Ala Ala Pro Glu Val Ile Ser Gly Arg Leu Tyr Ala Gly 180 185 190

Pro Glu Val Asp Ile Trp Ser Cys Gly Val Ile Leu Tyr Ala Leu Leu 195 200 205

Cys Gly Thr Leu Pro Phe Asp Asp Glu His Val Pro Thr Leu Phe Lys 210 215 220

Lys Ile Arg Gly Gly Val Phe Tyr Ile Pro Glu Tyr Leu Asn Arg Ser 225 230 235 240

Val Ala Thr Leu Leu Met His Met Leu Gln Val Asp Pro Leu Lys Arg \$245\$ \$250\$ \$255\$

Ala Thr Ile Lys Asp Ile Arg Glu His Glu Trp Phe Lys Gln Asp Leu 260 265 270

Pro Ser Tyr Leu Phe Pro Glu Asp Pro Ser Tyr Asp Ala Asn Val Ile 275 280 285

Asp Asp Glu Ala Val Lys Glu Val Cys Glu Lys Phe Glu Cys Thr Glu 290 295 300

Ser Glu Val Met Asn Ser Leu Tyr Ser Gly Asp Pro Gln Asp Gln Leu 305 310 315 320

Ala Val Ala Tyr His Leu Ile Ile Asp Asn Arg Arg Ile Met Asn Gln 325 330 335

Ala Ser Glu Phe Tyr Leu Ala Ser Ser Pro Pro Ser Gly Ser Phe Met

Asp Asp Ser Ala Met His Ile Pro Pro Gly Leu Lys Pro His Pro Glu 355 360 365

Arg Met Pro Pro Leu Ile Ala Asp Ser Pro Lys Ala Arg Cys Pro Leu 370 375 380

Asp Ala Leu Asn Thr Thr Lys Pro Lys Ser Leu Ala Val Lys Lys Ala 385 390 395 400

Lys Trp His Leu Gly Ile Arg Ser Gln Ser Lys Pro Tyr Asp Ile Met 405 410 415

Ala Glu Val Tyr Arg Ala Met Lys Gln Leu Asp Phe Glu Trp Lys Val 420 425 430

Val Asn Ala Tyr His Leu Arg Val Arg Arg Lys Asn Pro Val Thr Gly 435 440 445

Asn Tyr Val Lys Met Ser Leu Gln Leu Tyr Leu Val Asp Asn Arg Ser 450 460

Tyr Leu Leu Asp Phe Lys Ser Ile Asp Asp Glu Val Val Glu Gln Arg 465 470 475 480

Ser Gly Ser Ser Thr Pro Gln Arg Ser Cys Ser Ala Ala Gly Leu His  $485 \hspace{1.5cm} 490 \hspace{1.5cm} 495$ 

Arg Pro Arg Ser Ser Phe Asp Ser Thr Thr Ala Glu Ser His Ser Leu 500 505 510

Ser Gly Ser Leu Thr Gly Ser Leu Thr Gly Ser Thr Leu Ser Ser Val 515 520 525

Ser Pro Arg Leu Gly Ser His Thr Met Asp Phe Phe Glu Met Cys Ala 530 535 540

Ser Leu Ile Thr Thr Leu Ala Arg 545

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<213> Homo sapiens

<400> 6

Met Glu Val Val Asp Pro Gln Gln Leu Gly Met Phe Thr Glu Gly Glu 1 5 10 15

Leu Met Ser Val Gly Met Asp Thr Phe Ile His Arg Ile Asp Ser Thr 20 25 30

Glu Val Ile Tyr Gln Pro Arg Arg Lys Arg Ala Lys Leu Ile Gly Lys 35 40 45

Tyr Leu Met Gly Asp Leu Leu Gly Glu Gly Ser Tyr Gly Lys Val Lys 50 55 60

Glu Val Leu Asp Ser Glu Thr Leu Cys Arg Arg Ala Val Lys Ile Leu 65 70 75 80

Lys Lys Lys Leu Arg Arg Ile Pro Asn Gly Glu Ala Asn Val Lys 85 90 95

Lys Glu Ile Gln Leu Leu Arg Arg Leu Arg His Lys Asn Val Ile Gln 100 105 110

Leu Val Asp Val Leu Tyr Asn Glu Glu Lys Gln Lys Met Tyr Met Val 115 120 125

Met Glu Tyr Cys Val Cys Gly Met Gln Glu Met Leu Asp Ser Val Pro 130 135 140

Glu Lys Arg Phe Pro Val Cys Gln Ala His Gly Tyr Phe Cys Gln Leu 145 150 155 160

Ile Asp Gly Leu Glu Tyr Leu His Ser Gln Gly Ile Val His Lys Asp 165 170 175

Ile Lys Pro Gly Asn Leu Leu Leu Thr Thr Gly Gly Thr Leu Lys Ile 180 185 190 .

Ser Asp Leu Gly Val Ala Glu Ala Leu His Pro Phe Ala Ala Asp Asp 195 200 205

Thr Cys Arg Thr Ser Gln Gly Ser Pro Ala Phe Gln Pro Pro Glu Ile Ala Asn Gly Leu Asp Thr Phe Ser Gly Phe Lys Val Asp Ile Trp Ser Ala Gly Val Thr Leu Tyr Asn Ile Thr Thr Gly Leu Tyr Pro Phe Glu Gly Asp Asn Ile Tyr Lys Leu Phe Glu Asn Ile Gly Lys Gly Ser Tyr Ala Ile Pro Gly Asp Cys Gly Pro Pro Leu Ser Asp Leu Leu Lys Gly Met Leu Glu Tyr Glu Pro Ala Lys Arg Phe Ser Ile Arg Gln Ile Arg Gln His Ser Trp Phe Arg Lys Lys His Pro Pro Ala Glu Ala Pro Val Pro Ile Pro Pro Ser Pro Asp Thr Lys Asp Arg Trp Arg Ser Met Thr Val Val Pro Tyr Leu Glu Asp Leu His Gly Ala Asp Glu Asp Glu Asp Leu Phe Asp Ile Glu Asp Asp Ile Ile Tyr Thr Gln Asp Phe Thr Val Pro Gly Gln Val Pro Glu Glu Glu Ala Ser His Asn Gly Gln Arg Arg Gly Leu Pro Lys Ala Val Cys Met Asn Gly Thr Glu Ala Ala Gln Leu Ser Thr Lys Ser Arg Ala Glu Gly Arg Ala Pro Asn Pro Ala Arg Lys Ala Cys Ser Ala Ser Ser Lys Ile Arg Arg Leu Ser Ala Cys Lys Gln 

<210> 7 <211> 433 <212> PRT <213> Homo sapiens

<400> 7

Met Glu Val Val Asp Pro Gln Gln Leu Gly Met Phe Thr Glu Gly Glu 10

Leu Met Ser Val Gly Met Asp Thr Phe Ile His Arg Ile Asp Ser Thr

Glu Val Ile Tyr Gln Pro Arg Arg Lys Arg Ala Lys Leu Ile Gly Lys 40

Tyr Leu Met Gly Asp Leu Leu Gly Glu Gly Ser Tyr Gly Lys Val Lys

Glu Val Leu Asp Ser Glu Thr Leu Cys Arg Arg Ala Val Lys Ile Leu 70 75

Lys Lys Lys Leu Arg Arg Ile Pro Asn Gly Glu Ala Asn Val Lys 90

Lys Glu Ile Gln Leu Leu Arg Arg Leu Arg His Lys Asn Val Ile Gln

Leu Val Asp Val Leu Tyr Asn Glu Glu Lys Gln Lys Met Tyr Met Val 115 120

Met Glu Tyr Cys Val Cys Gly Met Gln Glu Met Leu Asp Ser Val Pro 130 135 140

Glu Lys Arg Phe Pro Val Cys Gln Ala His Gly Tyr Phe Cys Gln Leu 145 150 155

Ile Asp Gly Leu Glu Tyr Leu His Ser Gln Gly Ile Val His Lys Asp 165

Ile Lys Pro Gly Asn Leu Leu Thr Thr Gly Gly Thr Leu Lys Ile 180

Ser Asp Leu Gly Val Ala Glu Ala Leu His Pro Phe Ala Ala Asp Asp 195 200 205

Thr Cys Arg Thr Ser Gln Gly Ser Pro Ala Phe Gln Pro Pro Glu Ile 210  $\,$  220  $\,$ 

Ala Asn Gly Leu Asp Thr Phe Ser Gly Phe Lys Val Asp Ile Trp Ser 225 230 235 240

Ala Gly Val Thr Leu Tyr Asn Ile Thr Thr Gly Leu Tyr Pro Phe Glu 245 250 255

Gly Asp Asn Ile Tyr Lys Leu Phe Glu Asn Ile Gly Lys Gly Ser Tyr 260 265 270

Ala Ile Pro Gly Asp Cys Gly Pro Pro Leu Ser Asp Leu Leu Lys Gly 275 280 285

Met Leu Glu Tyr Glu Pro Ala Lys Arg Phe Ser Ile Arg Gln Ile Arg 290 295 300

Pro Ile Pro Pro Ser Pro Asp Thr Lys Asp Arg Trp Arg Ser Met Thr 325 330 335

Val Val Pro Tyr Leu Glu Asp Leu His Gly Ala Asp Glu Asp Glu Asp 340 345 350

Leu Phe Asp Ile Glu Asp Asp Ile Ile Tyr Thr Gln Asp Phe Thr Val 355 360 . 365

Pro Gly Gln Val Pro Glu Glu Glu Ala Ser His Asn Gly Gln Arg Arg 370 375 380

Gly Leu Pro Lys Ala Val Cys Met Asn Gly Thr Glu Ala Ala Gln Leu 385 390 395 400

Ser Thr Lys Ser Arg Ala Glu Gly Arg Ala Pro Asn Pro Ala Arg Lys 405 410 415

Ala Cys Ser Ala Ser Ser Lys Ile Arg Arg Leu Ser Ala Cys Lys Gln 420 425 430

Gln

<210> 8

<211> 433

<212> PRT

<213> Homo sapiens

<400> 8

Met Glu Val Val Asp Pro Gln Gln Leu Gly Met Phe Thr Glu Gly Glu
1 5 10 15

Leu Met Ser Val Gly Met Asp Thr Phe Ile His Arg Ile Asp Ser Thr 20 25 30

Glu Val Ile Tyr Gln Pro Arg Arg Lys Arg Ala Lys Leu Ile Gly Lys 35 40 45

Tyr Leu Met Gly Asp Leu Leu Gly Glu Gly Ser Tyr Gly Lys Val Lys 50 55 60

Glu Val Leu Asp Ser Glu Thr Leu Cys Arg Arg Ala Val Lys Ile Leu 65 70 75 80

Lys Lys Lys Leu Arg Arg Ile Pro Asn Gly Glu Ala Asn Val Lys 85 90 95

Lys Glu Ile Gln Leu Arg Arg Leu Arg His Lys Asn Val Ile Gln  $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$ 

Leu Val Asp Val Leu Tyr Asn Glu Glu Lys Gln Lys Met Tyr Met Val 115 120 125

Met Glu Tyr Cys Val Cys Gly Met Gln Glu Met Leu Asp Ser Val Pro 130 140

Glu Lys Arg Phe Pro Val Cys Gln Ala His Gly Tyr Phe Cys Gln Leu 145 150 155 160

Ile Asp Gly Leu Glu Tyr Leu His Ser Gln Gly Ile Val His Lys Asp 165 170 175 Ile Lys Pro Gly Asn Leu Leu Leu Thr Thr Gly Gly Thr Leu Lys Ile 180 185 190

Ser Asp Leu Gly Val Ala Glu Ala Leu His Pro Phe Ala Ala Asp Asp 195 200 205

Thr Cys Arg Thr Ser Gln Gly Ser Pro Ala Phe Gln Pro Pro Glu Ile 210 215 220

Ala Asn Gly Leu Asp Thr Phe Ser Gly Phe Lys Val Asp Ile Trp Ser 225 230 235 240

Ala Gly Val Thr Leu Tyr Asn Ile Thr Thr Gly Leu Tyr Pro Phe Glu 245 250 255

Gly Asp Asn Ile Tyr Lys Leu Phe Glu Asn Ile Gly Lys Gly Ser Tyr 260 265 270

Ala Ile Pro Gly Asp Cys Gly Pro Pro Leu Ser Asp Leu Leu Lys Gly 275 280 285

Met Leu Glu Tyr Glu Pro Ala Lys Arg Phe Ser Ile Arg Gln Ile Arg 290 295 300

Gln His Ser Trp Phe Arg Lys Lys His Pro Pro Ala Glu Ala Pro Val 305 310 315

Pro Ile Pro Pro Ser Pro Asp Thr Lys Asp Arg Trp Arg Ser Met Thr 325 330 335

Val Val Pro Tyr Leu Glu Asp Leu His Gly Ala Asp Glu Asp Glu Asp 340 345 350

Leu Phe Asp Ile Glu Asp Asp Ile Ile Tyr Thr Gln Asp Phe Thr Val 355 360 365

Pro Gly Gln Val Pro Glu Glu Glu Ala Ser His Asn Gly Gln Arg Arg 370 375 380

Gly Leu Pro Lys Ala Val Cys Met Asn Gly Thr Glu Ala Ala Gln Leu 385 390 395 400

Ser Thr Lys Ser Arg Ala Glu Gly Arg Ala Pro Asn Pro Ala Arg Lys 405 410 415

Ala Cys Ser Ala Ser Ser Lys Ile Arg Arg Leu Ser Ala Cys Lys Gln 420 425 430

Gln

<210> 9

<211> 431

<212> PRT

<213> Homo sapiens

<400> 9

Met Ser Phe Leu Val Ser Lys Pro Glu Arg Ile Arg Arg Trp Val Ser 1 5 10 15

Glu Lys Phe Ile Val Glu Gly Leu Arg Asp Leu Glu Leu Phe Gly Glu 20 25 30

Gln Pro Pro Gly Asp Thr Arg Arg Lys Thr Asn Asp Ala Ser Ser Glu 35 40 45

Ser Ile Ala Ser Phe Ser Lys Gln Glu Val Met Ser Ser Phe Leu Pro 50 55 60

Glu Gly Gly Cys Tyr Glu Leu Leu Thr Val Ile Gly Lys Gly Phe Glu 65 70 75 80

Asp Leu Met Thr Val Asn Leu Ala Arg Tyr Lys Pro Thr Gly Glu Tyr 85 90 95

Val Thr Val Arg Arg Ile Asn Leu Glu Ala Cys Ser Asn Glu Met Val 100 105 110

Thr Phe Leu Gln Gly Glu Leu His Val Ser Lys Leu Phe Asn His Pro 115 120 125

Asn Ile Val Pro Tyr Arg Ala Thr Phe Ile Ala Asp Asn Glu Leu Trp 130 135 140

Val Val Thr Ser Phe Met Ala Tyr Gly Ser Ala Lys Asp Leu Ile Cys

Thr His Phe Met Asp Gly Met Asn Glu Leu Ala Ile Ala Tyr Ile Leu 165 170 175

Gln Gly Val Leu Lys Ala Leu Asp Tyr Ile His His Met Gly Tyr Val 180 185 190

His Arg Ser Val Lys Ala Ser His Ile Leu Ile Ser Val Asp Gly Lys
195 200 205

Val Tyr Leu Ser Gly Leu Arg Ser Asn Leu Ser Met Ile Ser His Gly 210 215 220

Gln Arg Gln Arg Val Val His Asp Phe Pro Lys Tyr Ser Val Lys Val 225 230 235 240

Leu Pro Trp Leu Ser Pro Glu Val Leu Gln Gln Asn Leu Gln Gly Tyr
245 250 255

Asp Ala Lys Ser Asp Ile Tyr Ser Val Gly Ile Thr Ala Cys Glu Leu 260 265 270

Ala Asn Gly His Val Pro Phe Lys Asp Met Pro Ala Thr Gln Met Leu 275 280 285

Leu Glu Lys Leu Asn Gly Thr Val Pro Cys Leu Leu Asp Thr Ser Thr 290 295 300

Ile Pro Ala Glu Glu Leu Thr Met Ser Pro Ser Arg Ser Val Ala Asn 305 310 315 320

Ser Gly Leu Ser Asp Ser Leu Thr Thr Ser Thr Pro Arg Pro Ser Asn 325 330 335

Gly Asp Trp Pro Ser His Pro Tyr His Arg Thr Phe Ser Pro His Phe 340 345 350

His His Phe Val Glu Gln Cys Leu Gln Arg Asn Pro Asp Ala Arg Pro 355 360 365

Ser Ala Ser Thr Leu Leu Asn His Ser Phe Phe Lys Gln Ile Lys Arg 370 375 380 Arg Ala Ser Lys Ala Leu Pro Glu Leu Leu Arg Pro Val Thr Pro Ile 385 390 395 400

Thr Asn Phe Glu Gly Ser Gln Ser Gln Asp His Ser Gly Ile Phe Gly 405 410 415

Leu Val Thr Asn Leu Glu Glu Leu Glu Val Asp Asp Trp Glu Phe 420 425 430

<210> 10

<211> 418

<212> PRT

<213> Homo sapiens

<400> 10

Met Ser Leu Leu Asp Cys Phe Cys Thr Ser Arg Thr Gln Val Glu Ser  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Arg Pro Glu Lys Gln Ser Glu Thr Ser Ile His Gln Tyr Leu Val 20 25 30

Asp Glu Pro Thr Leu Ser Trp Ser Arg Pro Ser Thr Arg Ala Ser Glu 35 40 45

Val Leu Cys Ser Thr Asn Val Ser His Tyr Glu Leu Gln Val Glu Ile 50 60

Gly Arg Gly Phe Asp Asn Leu Thr Ser Val His Leu Ala Arg His Thr 65 70 75 80

Pro Thr Gly Thr Leu Val Thr Ile Lys Ile Thr Asn Leu Glu Asn Cys 85 90 95

Asn Glu Glu Arg Leu Lys Ala Leu Gln Lys Ala Val Ile Leu Ser His  $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$ 

Phe Phe Arg His Pro Asn Ile Thr Thr Tyr Trp Thr Val Phe Thr Val 115 120 125

Gly Ser Trp Leu Trp Val Ile Ser Pro Phe Met Ala Tyr Gly Ser Ala 130 135 140

Ser Gln Leu Leu Arg Thr Tyr Phe Pro Glu Gly Met Ser Glu Thr Leu 145 150 Ile Arg Asn Ile Leu Phe Gly Ala Val Arg Gly Leu Asn Tyr Leu His 170 Gln Asn Gly Cys Ile His Arg Ser Ile Lys Ala Ser His Ile Leu Ile 185 Ser Gly Asp Gly Leu Val Thr Leu Ser Gly Leu Ser His Leu His Ser 200 Leu Val Lys His Gly Gln Arg His Arg Ala Val Tyr Asp Phe Pro Gln 215 Phe Ser Thr Ser Val Gln Pro Trp Leu Ser Pro Glu Leu Leu Arg Gln Asp Leu His Gly Tyr Asn Val Lys Ser Asp Ile Tyr Ser Val Gly Ile 250 Thr Ala Cys Glu Leu Ala Ser Gly Gln Val Pro Phe Gln Asp Met His Arg Thr Gln Met Leu Gln Lys Leu Lys Gly Pro Pro Tyr Ser Pro 280 Leu Asp Ile Ser Ile Phe Pro Gln Ser Glu Ser Arg Met Lys Asn Ser 290 295 300 Gln Ser Gly Val Asp Ser Gly Ile Gly Glu Ser Val Leu Val Ser Ser 305 310 315 320 Gly Thr His Thr Val Asn Ser Asp Arg Leu His Thr Pro Ser Ser Lys 325 330 335 Thr Phe Ser Pro Ala Phe Phe Ser Leu Val Gln Leu Cys Leu Gln Gln 340 Asp Pro Glu Lys Arg Pro Ser Ala Ser Ser Leu Leu Ser His Val Phe 355 360 365 Phe Lys Gln Met Lys Glu Glu Ser Gln Asp Ser Ile Leu Ser Leu Leu

Pro Pro Ala Tyr Asn Lys Pro Ser Ile Ser Leu Pro Pro Val Leu Pro 385 390 395 400

Trp Thr Glu Pro Glu Cys Asp Phe Pro Asp Glu Lys Asp Ser Tyr Trp 405 410 415

Glu Phe

<210> 11

<211> 341

<212> PRT

<213> Homo sapiens

<400> 11

Met Pro Phe Pro Phe Gly Lys Ser His Lys Ser Pro Ala Asp Ile Val 1 5 10 15

Lys Asn Leu Lys Glu Ser Met Ala Val Leu Glu Lys Gln Asp Ile Ser 20 25 30

Asp Lys Lys Ala Glu Lys Ala Thr Glu Glu Val Ser Lys Asn Leu Val 35 40 45

Ala Met Lys Glu Ile Leu Tyr Gly Thr Asn Glu Lys Glu Pro Gln Thr 50 55 60

Glu Ala Val Ala Gln Leu Ala Gln Glu Leu Tyr Asn Ser Gly Leu Leu 65 70 75 80

Ser Thr Leu Val Ala Asp Leu Gln Leu Ile Asp Phe Glu Gly Lys Lys
85 90 95

Asp Val Ala Gln Ile Phe Asn Asn Ile Leu Arg Arg Gln Ile Gly Thr 100 105 110

Arg Thr Pro Thr Val Glu Tyr Ile Cys Thr Gln Gln Asn Ile Leu Phe 115 120 125

Met Leu Leu Lys Gly Tyr Glu Ser Pro Glu Ile Ala Leu Asn Cys Gly 130 135

165 170 175

Thr Phe Asp Ile Ala Ser Asp Ala Phe Ala Thr Phe Lys Asp Leu Leu 180 185 190

Thr Arg His Lys Leu Leu Ser Ala Glu Phe Leu Glu Gln His Tyr Asp 195 200 205

Arg Phe Phe Ser Glu Tyr Glu Lys Leu Leu His Ser Glu Asn Tyr Val 210 215 220

Thr Lys Arg Gln Ser Leu Lys Leu Leu Gly Glu Leu Leu Leu Asp Arg 225 230 235 240

His Asn Phe Thr Ile Met Thr Lys Tyr Ile Ser Lys Pro Glu Asn Leu 245 250 255

Lys Leu Met Met Asn Leu Leu Arg Asp Lys Ser Arg Asn Ile Gln Phe 260 265 270

Glu Ala Phe His Val Phe Lys Val Phe Val Ala As<br/>n Pro As<br/>n Lys Thr275 280 285

Gln Pro Ile Leu Asp Ile Leu Leu Lys Asn Gln Ala Lys Leu Ile Glu 290 295 300

Phe Leu Ser Lys Phe Gln Asn Asp Arg Thr Glu Asp Glu Gln Phe Asn 305 310 315 320

Asp Glu Lys Thr Tyr Leu Val Lys Gln Ile Arg Asp Leu Lys Arg Pro 325 330 335

Ala Gln Gln Glu Ala 340

<210> 12

<211> 337

<212> PRT

<213> Homo sapiens

<400> 12

Met Lys Lys Met Pro Leu Phe Ser Lys Ser His Lys Asn Pro Ala Glu  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$ 

Ile Val Lys Ile Leu Lys Asp Asn Leu Ala Ile Leu Glu Lys Gln Asp 20 25 30

Lys Lys Thr Asp Lys Ala Ser Glu Glu Val Ser Lys Ser Leu Gln Ala 35 40 45

Met Lys Glu Ile Leu Cys Gly Thr Asn Glu Lys Glu Pro Pro Thr Glu 50 60

Ala Val Ala Gln Leu Ala Gln Glu Leu Tyr Ser Ser Gly Leu Leu Val 65 70 75 80

Thr Leu Ile Ala Asp Leu Gln Leu Ile Asp Phe Glu Gly Lys Lys Asp 85 90 95

Val Thr Gln Ile Phe Asn Asn Ile Leu Arg Arg Gln Ile Gly Thr Arg 100 105 110

Ser Pro Thr Val Glu Tyr Ile Ser Ala His Pro His Ile Leu Phe Met 115 120 125

Leu Leu Lys Gly Tyr Glu Ala Pro Gln Ile Ala Leu Arg Cys Gly Ile 130 135 140

Phe Ser Asn Gln Phe Arg Asp Phe Phe Lys Tyr Val Glu Leu Ser Thr 165 170 175

Phe Asp Ile Ala Ser Asp Ala Phe Ala Thr Phe Lys Asp Leu Leu Thr 180 185 190

Arg His Lys Val Leu Val Ala Asp Phe Leu Glu Gln Asn Tyr Asp Thr 195 200 205

Ile Phe Glu Asp Tyr Glu Lys Leu Leu Gln Ser Glu Asn Tyr Val Thr 210 215 220

Lys Arg Gln Ser Leu Lys Leu Gly Glu Leu Ile Leu Asp Arg His 235 ·

Asn Phe Ala Ile Met Thr Lys Tyr Ile Ser Lys Pro Glu Asn Leu Lys 250

Leu Met Met Asn Leu Leu Arg Asp Lys Ser Pro Asn Ile Gln Phe Glu 260 265

Ala Phe His Val Phe Lys Val Phe Val Ala Ser Pro His Lys Thr Gln 280

Pro Ile Val Glu Ile Leu Leu Lys Asn Gln Pro Lys Leu Ile Glu Phe 295

Leu Ser Ser Phe Gln Lys Glu Arg Thr Asp Asp Glu Gln Phe Ala Asp

Glu Lys Asn Tyr Leu Ile Lys Gln Ile Arg Asp Leu Lys Lys Thr Ala

Pro

<210> 13

<211> 338 <212> PRT

<213> Caenorhabditis elegans

<400> 13

Met Leu Lys Pro Leu Phe Gly Lys Ala Asp Lys Thr Pro Ala Asp Val 1.0

Val Lys Asn Leu Arg Asp Ala Leu Leu Val Ile Asp Arg His Gly Thr 20 25

Asn Thr Ser Glu Arg Lys Val Glu Lys Ala Ile Glu Glu Thr Ala Lys

Met Leu Ala Leu Ala Lys Thr Phe Ile Tyr Gly Ser Asp Ala Asn Glu 55

Pro Asn Asn Glu Gln Val Thr Gln Leu Ala Gln Glu Val Tyr Asn Ala 65 70 75 80

Asn Val Leu Pro Met Leu Ile Lys His Leu His Lys Phe Glu Phe Glu 85 90 95

Cys Lys Lys Asp Val Ala Ser Val Phe Asn Asn Leu Leu Arg Arg Gln 100 105 110

Ile Gly Thr Arg Ser Pro Thr Val Glu Tyr Leu Ala Ala Arg Pro Glu 115 120 125

Ile Leu Ile Thr Leu Leu Gly Tyr Glu Gln Pro Asp Ile Ala Leu 130 135 140

Thr Cys Gly Ser Met Leu Arg Glu Ala Val Arg His Glu His Leu Ala 145  $\phantom{\bigg|}$  150  $\phantom{\bigg|}$  155  $\phantom{\bigg|}$  160

Arg Ile Val Leu Tyr Ser Glu Tyr Phe Gln Arg Phe Phe Val Phe Val 165 170 175

Gln Ser Asp Val Phe Asp Ile Ala Thr Asp Ala Phe Ser Thr Phe Lys 180 185 190

Asp Leu Met Thr Lys His Lys Asn Met Cys Ala Glu Tyr Leu Asp Asn 195 200 205

Asn Tyr Asp Arg Phe Phe Gly Gln Tyr Ser Ala Leu Thr Asn Ser Glu 210 215 220

Asn Tyr Val Thr Arg Arg Gln Ser Leu Lys Leu Leu Gly Glu Leu Leu 225 230 235 240

Leu Asp Arg His Asn Phe Ser Thr Met Asn Lys Tyr Ile Thr Ser Pro 245 250 255

Glu Asn Leu Lys Thr Val Met Glu Leu Leu Arg Asp Lys Arg Asn 260 265 270

Ile Gln Tyr Glu Ala Phe His Val Phe Lys Ile Phe Val Ala Asn Pro 275 280 285

Asn Lys Pro Arg Pro Ile Thr Asp Ile Leu Thr Arg Asn Arg Asp Lys

290 295 300

Leu Val Glu Phe Leu Thr Ala Phe His Asn Asp Arg Thr Asn Asp Glu 305 310 315 320

Gln Phe Asn Asp Glu Lys Ala Tyr Leu Ile Lys Gln Ile Gln Glu Leu
325 330 335

Arg Val

<210> 14

<211> 636

<212> PRT

<213> Caenorhabditis elegans

<400> 14

Met Asp Ser Thr Thr Ser Leu Pro Asn Asn Val Leu Leu Lys Lys Ala 1 5 10 15

Arg Pro Ser Lys Ile Phe Ala Val Thr Ser Ala Asn Ala Leu Asn Val 20 25 30

Lys Thr Glu Pro Val Ile Phe Val Lys Ser Asp Asp Leu Asn Gln Ala 35 40 . 45

Asn Thr Pro Leu Thr Gly Ser Lys Phe Gly Thr His Leu Ala Cys Ile 50 55 60

Arg Thr Ser Cys Leu His Arg Thr Val Asn Ala Ser Asn Tyr Ser Thr 65 70 75 80

Met Ser Asp Gly Gly Leu Tyr Thr Ser Asp Glu Pro Cys Ser Ser Ala 85 90 . 95

Gln Ala Glu Phe Arg Leu Ala Ala His Trp Glu Ser Thr Phe Thr Arg 100 105 110

Thr Arg Glu Ile His Cys Asp Thr Gly Tyr Ser Ser Gln Ser Pro Pro 115 120 125

Glu Thr Thr Val Phe Ile Gln Lys Ser Arg Phe Pro Val Ala Glu Lys 130 135 140

Pro Gly Thr Pro Glu Leu Lys Ser Phe Glu Ser Lys Leu Val Gln 150 Lys Lys Ser Gly Asn Ala Ser Thr Pro Thr Arg Lys Leu Ala Ser Glu 170 Glu Lys Lys Ala Lys Asn Thr Ser Met Gly Gln Thr Pro Ser Lys Leu 180 185 Lys Ser Pro Lys Ala Leu Lys Met Val Lys Lys Glu Asn Glu Pro Ala 200 195 Ile Pro Pro Asn His Phe Glu Gly Lys Val Tyr Gly Tyr Leu Val Asp 210 215 Asp Met Ser Ala Ile Gly Ile Gln Pro Ile Leu Asp Lys Tyr Asn Glu 230 Asp Pro Glu Lys Phe Phe Lys Arg Phe Asp Ser Lys Pro Trp Phe Arg Arg Lys Val Met Pro Leu Leu Phe Gly Lys Ser His Lys Ser Pro Ala 260 265 Asp Val Val Lys Thr Leu Arg Glu Val Leu Thr Ile Leu Asp Lys Leu 280 Pro Pro Pro Lys Leu Asp Lys Asp Gly Asn Ile Gln Ser Asp Lys Lys 295 Tyr Asp Lys Ala Leu Asp Glu Val Ser Lys Asn Val Ala Met Ile Lys 305 310 315 Ser Phe Ile Tyr Gly Asn Asp Ser Ala Glu Pro Ser Ser Glu His Val 325 330 Val Gln Val Ala Gln Leu Ala Gln Glu Val Tyr Asn Ala Asn Ile Leu 345 Pro Met Leu Ile Lys Met Leu Pro Lys Phe Glu Phe Glu Cys Lys Lys 360

Asp Val Gly Gln Ile Phe Asn Asn Leu Leu Arg Arg Gln Ile Gly Thr 370 380

Arg Ser Pro Thr Val Glu Tyr Leu Gly Ala Arg Pro Glu Ile Leu Ile 385 390 395 400

Gln Leu Val Gln Gly Tyr Ser Val Pro Asp Ile Ala Leu Thr Cys Gly
405 410 415

Leu Met Leu Arg Glu Ser Ile Arg His Asp His Leu Ala Lys Ile Ile 420 425 430

Leu Tyr Ser Asp Val Phe Tyr Thr Phe Phe Leu Tyr Val Gln Ser Glu 435 440 445

Val Phe Asp Ile Ser Ser Asp Ala Phe Ser Thr Phe Lys Glu Leu Thr 450 455 460

Thr Arg His Lys Ala Ile Ile Ala Glu Phe Leu Asp Ser Asn Tyr Asp 465 470 475 480

Thr Phe Phe Ala Gln Tyr Gln Asn Leu Leu Asn Ser Lys Asn Tyr Val 485 490 495

Thr Arg Arg Gln Ser Leu Lys Leu Leu Gly Glu Leu Leu Leu Asp Arg 500 505 510

His Asn Phe Asn Thr Met Thr Lys Tyr Ile Ser Asn Pro Asp Asn Leu 515 520 525

Arg Leu Met Met Glu Leu Leu Arg Asp Lys Ser Arg Asn Ile Gln Tyr 530 540

Glu Ala Phe His Val Phe Lys Val Phe Val Ala Asn Pro Asn Lys Pro 545 550 555 560

Lys Pro Ile Ser Asp Ile Leu Asn Arg Asn Arg Glu Lys Leu Val Glu 565 570 575

Phe Leu Ser Glu Phe His Asn Asp Arg Thr Asp Asp Glu Gln Phe Asn 580 585 590

Asp Glu Lys Ala Tyr Leu Ile Lys Gln Ile Gln Glu Met Lys Ser Ser

595 600 605

Pro Lys Glu Ala Lys Lys Pro Lys Ser Lys Glu Asp Glu Asn Gln Glu 610 615 620

Pro Ala Gly Pro Ser Glu Gly Pro Ser Thr Ser Gln 625 630 635

<210> 15

<211> 339

<212> PRT

<213> Drosophila melanogaster

<400> 15

Met Pro Leu Phe Gly Lys Ser Gln Lys Ser Pro Val Glu Leu Val Lys 1  $\phantom{\bigg|}$  5  $\phantom{\bigg|}$  10  $\phantom{\bigg|}$  15

Ser Leu Lys Glu Ala Ile Asn Ala Leu Glu Ala Gly Asp Arg Lys Val $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Glu Lys Ala Gln Glu Asp Val Ser Lys Asn Leu Val Ser Ile Lys Asn 35 40 45

Met Leu Tyr Gly Ser Ser Asp Ala Glu Pro Pro Ala Asp Tyr Val Val 50 55 60

Ala Gln Leu Ser Gln Glu Leu Tyr Asn Ser Asn Leu Leu Leu Leu 65 70 75 80

Ile Gln Asn Leu His Arg Ile Asp Phe Glu Gly Lys Lys His Val Ala 85 90 95

Leu Ile Phe Asn Asn Val Leu Arg Gln Ile Gly Thr Arg Ser Pro 100 105 110

Thr Val Glu Tyr Ile Cys Thr Lys Pro Glu Ile Leu Phe Thr Leu Met 115 120 125

Ala Gly Tyr Glu Asp Ala His Pro Glu Ile Ala Leu Asn Ser Gly Thr 130 135 140

Met Leu Arg Glu Cys Ala Arg Tyr Glu Ala Leu Ala Lys Ile Met Leu 145 150 155 160

His Ser Asp Glu Phe Phe Lys Phe Phe Arg Tyr Val Glu Val Ser Thr 165 170  $\cdot$  175

Phe Asp Ile Ala Ser Asp Ala Phe Ser Thr Phe Lys Glu Leu Leu Thr 180 185 190

Arg His Lys Leu Cus Ala Glu Phe Leu Asp Ala Asn Tyr Asp Lys
195 200 205

Phe Phe Ser Gln His Tyr Gln Arg Leu Leu Asn Ser Glu Asn Tyr Val 210 215 220

Thr Arg Arg Gln Ser Leu Lys Leu Leu Gly Glu Leu Leu Leu Asp Arg 225 230 235 240

His Asn Phe Thr Val Met Thr Arg Tyr Ile Ser Glu Pro Glu Asn Leu 245 250 255

Lys Leu Met Met Asn Met Leu Lys Glu Lys Ser Arg Asn Ile Gln Phe 260 265 270

Glu Ala Phe His Val Phe Lys Val Phe Val Ala Asn Pro Asn Lys Pro 275 280 285

Lys Pro Ile Leu Asp Ile Leu Leu Arg Asn Gln Thr Lys Leu Val Asp 290 295 300

Phe Leu Thr Asn Phe His Thr Asp Arg Ser Glu Asp Glu Gln Phe Asn 305 310 315 320

Asp Glu Lys Ala Tyr Leu Ile Lys Gln Ile Lys Glu Leu Lys Pro Leu 325 330 335

Pro Glu Ala

<210> 16

<211> 20

<212> PRT

<213> Artificial

<220>

<223> LKB1 substrate

```
<400> 16
Leu Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly
                                  10
Ser Pro Leu Tyr
 20
<210> 17
<211>
      20
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 17
Phe Gly Asn Phe Tyr Lys Ser Gly Glu Pro Leu Ser Thr Trp Cys Gly
Ser Pro Pro Tyr
           20
<210> 18
<211> 20
<212> PRT
<213>
      Artificial
<220>
<223> LKB1 substrate
<400> 18
Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys Gly
               5
                                   10
Ser Pro Asn Tyr
           20
<210> 19
<211> 20
<212> PRT
<213> Artificial
<220>
<223>
     LKB1 substrate
<400> 19
```

Met Ala Ser Leu Gln Val Gly Asp Ser Leu Leu Glu Thr Ser Cys Gly

```
10 15
```

Ser Pro His Tyr 20

<210> 20

<211> 20

<212> PRT

<213> Artificial

<220>

<223> LKB1 substrate

<400> 20

Phe Ser Asn Glu Phe Thr Val Gly Gly Lys Leu Asp Thr Phe Cys Gly 1 5 10 15

Ser Pro Pro Tyr 20

<210> 21

<211> 20

<212> PRT

<213> Artificial

<220>

<223> LKB1 substrate

<400> 21

Ala Lys Pro Lys Gly Asn Lys Asp Tyr His Leu Gln Thr Cys Cys Gly 1 5 10 15

Ser Leu Ala Tyr 20

<210> 22

<211> 20

<212> PRT

<213> Artificial

<220>

<223> LKB1 substrate

<400> 22

Leu Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly 1 5 10 15

```
Ser Pro Leu Tyr
            20
 <210> 23
 <211> 23
 <212> PRT
 <213> Artificial
<220>
<223> LKB1 substrate
 <400> 23
Leu Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly
 Ser Pro Leu Tyr Arg Arg Arg
            20
 <210> 24
 <211> 19
 <212> PRT
 <213> Artificial
 <220>
 <223> LKB1 substrate
 <400> 24
 Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly Ser
                5
Pro Leu Tyr
 <210> 25
 <211> 22
 <212> PRT
 <213> Artificial
<223> LKB1 substrate
 <400> 25
Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly Ser
                5
                                                        15
. Pro Leu Tyr Arg Arg Arg
```

20

```
<210> 26
<211> 20
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 26
Leu Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly
                                    10
Ser Pro Leu Tyr
            20
<210> 27
<211> 23
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 27
Leu Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly
Ser Pro Leu Tyr Arg Arg Arg
<210> 28
<211> 20
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 28
Phe Gly Asn Phe Tyr Lys Ser Gly Glu Pro Leu Ser Thr Trp Cys Gly
                                    10
Ser Pro Pro Tyr
       . 20
<210> 29
<211> 23
```

```
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 29
Phe Gly Asn Phe Tyr Lys Ser Gly Glu Pro Leu Ser Thr Trp Cys Gly
Ser Pro Pro Tyr Arg Arg Arg
 20 .
<210> 30
<211> 20
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 30
Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys Gly
Ser Pro Asn Tyr
  20
<210> 31
<211> 23
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 31
Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys Gly
                5
                                                        15
Ser Pro Asn Tyr Arg Arg Arg
            20
<210> 32
<211> 20
<212> PRT
<213> Artificial
```

```
<220>
 <223> LKB1 substrate
 <400> 32
 Met Ala Ser Leu Gln Val Gly Asp Ser Leu Leu Glu Thr Ser Cys Gly
 Ser Pro His Tyr
             20
 <210> 33
 <211> 23
 <212> PRT
 <213> Artificial
 <220>
 <223> LKB1 substrate
 <400> 33
 Met Ala Ser Leu Gln Val Gly Asp Ser Leu Leu Glu Thr Ser Cys Gly
 Ser Pro His Tyr Arg Arg Arg
             20
 <210> 34
       20
 <211>
       PRT
 <212>
 <213> Artificial
 <220>
 <223> LKB1 substrate
<400> 34
 Phe Ser Asn Glu Phe Thr Val Gly Gly Lys Leu Asp Thr Phe Cys Gly
                                     10
 Ser Pro Pro Tyr
             20
 <210> 35
 <211> 23
 <212> PRT
 <213> Artificial
 <220>
 <223> LKB1 substrate
```

```
<400> 35
Phe Ser Asn Glu Phe Thr Val Gly Gly Lys Leu Asp Thr Phe Cys Gly
Ser Pro Pro Tyr Arg Arg Arg
            20
<210> 36
<211> 20
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 36
Ala Lys Pro Lys Gly Asn Lys Asp Tyr His Leu Gln Thr Cys Cys Gly
Ser Leu Ala Tyr
 20
<210> 37
<211> 23
<212> PRT
<213> Artificial
<220>
<223> LKB1 substrate
<400> 37
Ala Lys Pro Lys Gly Asn Lys Asp Tyr His Leu Gln Thr Cys Cys Gly
               5
                                   10
Ser Leu Ala Tyr Arg Arg Arg
           20
<210> 38
<211> 19
<212> PRT
<213> Homo sapiens
<400> 38
Met Val Ala Gly Leu Thr Leu Gly Lys Gly Pro Glu Ser Pro Asp Gly
```

10

```
Asp Val Ser
<210>
       39
<211>
      20
<212> PRT
<213> Homo sapiens
<400> 39
Leu Ser Trp Gly Ala Gly Leu Lys Gly Gln Lys Val Ala Thr Ser Tyr
                                   10
Glu Ser Ser Leu
<210>
      40
<211>
      21
<212>
      PRT
<213>
      Homo sapiens
<400> 40
Met Glu Gly Ala Ala Pro Val Ala Gly Asp Arg Pro Asp Leu Gly
                                   10
Leu Gly Ala Pro Gly
<210>
      41
      21
<211>
<212>
      PRT
<213> Homo sapiens
<400> 41
Thr Asp Cys Gln Glu Val Thr Ala Thr Tyr Arg Gln Ala Leu Arg Val
                                   10
Cys Ser Lys Leu Thr
<210> 42
<211> 21
<212> PRT
<213> Homo sapiens
<400> 42
```

Met Val Met Ala Asp Gly Pro Arg His Leu Gln Arg Gly Pro Val Arg

10 15

Val Gly Phe Tyr Asp 20

<210> 43 <211> 20

1

<212> PRT

<213> Homo sapiens

<400> 43

Met Val Ile Met Ser Glu Phe Ser Ala Asp Pro Ala Gly Gln Gly Gln 1 5 10 15

Gly Gln Gln Lys 20

<210> 44

<211> 20

<212> PRT

<213> Homo sapiens

<400> 44

Gly Asp Cys Glu Met Glu Asp Leu Met Pro Cys Ser Leu Gly Thr Phe 1  $\phantom{-}$  5  $\phantom{-}$  10  $\phantom{-}$  15

Val Leu Val Gln

<210> 45

<211> 21

<212> PRT

<213> Homo sapiens

<400> 45

Thr Asp Ile Leu Leu Ser Tyr Lys His Pro Glu Val Ser Phe Ser Met 1  $\phantom{\bigg|}$  5  $\phantom{\bigg|}$  10  $\phantom{\bigg|}$  15

Glu Gln Ala Gly Val 20

<210> 46

<211> 20

<212> PRT

<213> Homo sapiens

```
<400> 46
Ser Gly Thr Ser Ile Ala Phe Lys Asn Ile Ala Ser Lys Ile Ala Asn
Glu Leu Lys Leu
        20
<210> 47
<211> 20
<212> PRT
<213> Homo sapiens
<400> 47
Met Ser Ser Arg Thr Val Leu Ala Pro Gly Asn Asp Arg Asn Ser Asp
                                   10
Thr His Gly Thr
<210> 48
<211> 20
<212> PRT
<213> Homo sapiens
<400> 48
Met Lys Asp Tyr Asp Glu Leu Leu Lys Tyr Tyr Glu Leu His Glu Thr
Ile Gly Thr Gly
           20
<210> 49
<211> 16
<212> PRT
<213> Homo sapiens
<400> 49
Cys Thr Ser Pro Pro Asp Ser Phe Leu Asp Asp His His Leu Thr Arg
                                   10
<210> 50
<211> 14
<212> PRT
<213> Homo sapiens
<400> 50
```

```
Cys Asp Pro Met Lys Arg Ala Thr Ile Lys Asp Ile Arg Glu
<210> .51
<211>
      12
<212> PRT
<213> Artificial
<220>
<223> C-terminal 12 residues STRAD alpha
<400> 51
Asn Leu Glu Glu Leu Glu Val Asp Asp Trp Glu Phe
<210> 52
<211>
      12
<212> PRT
<213> Artificial
<220>
<223> C-terminal 12 residues STRAD alpha, last residue mutated to Ala
<400> 52
Asn Leu Glu Glu Leu Glu Val Asp Asp Trp Glu Ala
<210> 53
<211>
      12
<212>
      PRT
<213> Artificial
<220>
<223> C-terminal 12 residues STRAD alpha, third last residue mutated t
       o Ala
<400> 53
Asn Leu Glu Glu Leu Glu Val Asp Asp Ala Glu Phe
                5
<210> 54
<211>
      12
<212> PRT
<213> Artificial
<220>
<223> C-terminal 12 residues STRAD alpha, second last residue mutated t
       o Ala
```

```
<400> 54
```

<210> 55

<211> 6

<212> PRT

<213> Artificial

<220>

<223> C-terminal 6 residues STRAD alpha

<400> 55

Val Asp Asp Trp Glu Phe
1 5

<210> 56

<211> 547

<212> PRT

<213> Homo sapiens

<400> 56

Met Ala Glu Pro Ser Gly Ser Pro Val His Val Gln Leu Pro Gln Gln  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Ala Ala Pro Val Thr Ala Ala Ala Ala Ala Pro Ala Ala Thr 20 25 30

Ala Ala Pro Ala Pro Ala Ala Pro Ala Pro Ala Pro Ala Pro Ala 35 40 45

Pro Ala Pro Ala Ala Gln Ala Val Gly Trp Pro Ile Cys Arg Asp Ala 50 55 60

Tyr Glu Leu Gln Glu Val Ile Gly Ser Gly Ala Thr Ala Val Val Gln 65 70 75 80

Ala Ala Leu Cys Lys Pro Arg Gln Glu Arg Val Ala Ile Lys Arg Ile 85 90 95

Asn Leu Glu Lys Cys Gln Thr Ser Met Asp Glu Leu Leu Lys Glu Ile 100 105 110

Gln Ala Met Ser Gln Cys Ser His Pro Asn Val Val Thr Tyr Tyr Thr 115 120 125

Ser Phe Val Val Lys Asp Glu Leu Trp Leu Val Met Lys Leu Leu Ser Gly Gly Ser Met Leu Asp Ile Ile Lys Tyr Ile Val Asn Arg Gly Glu His Lys Asn Gly Val Leu Glu Glu Ala Ile Ile Ala Thr Ile Leu Lys Glu Val Leu Glu Gly Leu Asp Tyr Leu His Arg Asn Gly Gln Ile His Arg Asp Leu Lys Ala Gly Asn Ile Leu Leu Gly Glu Asp Gly Ser Val Gln Ile Ala Asp Phe Gly Val Ser Ala Phe Leu Ala Thr Gly Gly Asp Val Thr Arg Asn Lys Val Arg Lys Thr Phe Val Gly Thr Pro Cys Trp Met Ala Pro Glu Val Met Glu Gln Val Arg Gly Tyr Asp Phe Lys Ala Asp Met Trp Ser Phe Gly Ile Thr Ala Ile Glu Leu Ala Thr Gly Ala Ala Pro Tyr His Lys Tyr Pro Pro Met Lys Val Leu Met Leu Thr Leu Gln Asn Asp Pro Pro Thr Leu Glu Thr Gly Val Glu Asp Lys Glu Met Met Lys Lys Tyr Gly Lys Ser Phe Arg Lys Leu Leu Ser Leu Cys Leu Gln Lys Asp Pro Ser Lys Arg Pro Thr Ala Ala Glu Leu Leu Lys Cys Lys Phe Phe Gln Lys Ala Lys Asn Arg Glu Tyr Leu Ile Glu Lys Leu

Leu Thr Arg Thr Pro Asp Ile Ala Gln Arg Ala Lys Lys Val Arg Arg 355 360 365

Val Pro Gly Ser Ser Gly His Leu His Lys Thr Glu Asp Gly Asp Trp 370 375 380

Glu Trp Ser Asp Asp Glu Met Asp Glu Lys Ser Glu Glu Gly Lys Ala 385 390 395 400

Ala Phe Ser Gl<br/>n Glu Lys Ser Arg Arg Val Lys Glu Glu As<br/>n Pro Glu 405  $\phantom{000}410\phantom{000}$  410  $\phantom{0000}415\phantom{000}$ 

Ile Ala Val Ser Ala Ser Thr Ile Pro Glu Gln Ile Gln Ser Leu Ser 420 425 430

Val His Asp Ser Gln Gly Pro Pro Asn Ala Asn Glu Asp Tyr Arg Glu 435 440 445

Ala Ser Ser Cys Ala Val Asn Leu Val Leu Arg Leu Arg Asn Ser Arg 450 460

Lys Glu Leu Asn Asp Ile Arg Phe Glu Phe Thr Pro Gly Arg Asp Thr 465 470 475 480

Ala Asp Gly Val Ser Gln Glu Leu Phe Ser Ala Gly Leu Val Asp Gly 485 490 495

His Asp Val Val Ile Val Ala Ala Asn Leu Gln Lys Ile Val Asp Asp 500 505 510

Pro Lys Ala Leu Lys Thr Leu Thr Phe Lys Leu Ala Ser Gly Cys Asp 515 520 525

Gly Ser Glu Ile Pro Asp Glu Val Lys Leu Ile Gly Phe Ala Gln Leu 530 540

Ser Val Ser 545

<210> 57 <211> 527

<212> PRT

<213> Homo sapiens

<400> 57

Met Ser Glu Asp Ser Ser Ala Leu Pro Trp Ser Ile Asn Arg Asp Asp 1 5 10 15

Tyr Glu Leu Gl<br/>n Glu Val Ile Gly Ser Gly Ala Thr Ala Val Val Gl<br/>n 20 25 30

Ala Ala Tyr Cys Ala Pro Lys Lys Glu Lys Val Ala Ile Lys Arg Ile 35 40 45

Asn Leu Glu Lys Cys Gln Thr Ser Met Asp Glu Leu Leu Lys Glu Ile 50 55 60

Gln Ala Met Ser Gln Cys His His Pro Asn Ile Val Ser Tyr Tyr Thr 65 70 75 80

Ser Phe Val Val Lys Asp Glu Leu Trp Leu Val Met Lys Leu Leu Ser 85 90 95

Gly Gly Ser Val Leu Asp Ile Ile Lys His Ile Val Ala Lys Gly Glu  $100 \hspace{1cm} 105 \hspace{1cm} 110$ 

His Lys Ser Gly Val Leu Asp Glu Ser Thr Ile Ala Thr Ile Leu Arg 115 120 125

Glu Val Leu Glu Gly Leu Glu Tyr Leu His Lys Asn Gly Gln Ile His 130 135 140

Arg Asp Val Lys Ala Gly Asn Ile Leu Leu Gly Glu Asp Gly Ser Val 145 150 155 160

Gln Ile Ala Asp Phe Gly Val Ser Ala Phe Leu Ala Thr Gly Gly Asp 165 170 175

Ile Thr Arg Asn Lys Val Arg Lys Thr Phe Val Gly Thr Pro Cys Trp
180 185 190

Met Ala Pro Glu Val Met Glu Gln Val Arg Gly Tyr Asp Phe Lys Ala 195 200 205

Asp Ile Trp Ser Phe Gly Ile Thr Ala Ile Glu Leu Ala Thr Gly Ala 210 220

Ala Pro Tyr His Lys Tyr Pro Pro Met Lys Val Leu Met Leu Thr Leu Gln Asn Asp Pro Pro Ser Leu Glu Thr Gly Val Gln Asp Lys Glu Met Leu Lys Lys Tyr Gly Lys Ser Phe Arg Lys Met Ile Ser Leu Cys Leu Gln Lys Asp Pro Glu Lys Arg Pro Thr Ala Ala Glu Leu Leu Arg His Lys Phe Phe Gln Lys Ala Lys Asn Lys Glu Phe Leu Gln Glu Lys Thr Leu Gln Arg Ala Pro Thr Ile Ser Glu Arg Ala Lys Lys Val Arg Arg Val Pro Gly Ser Ser Gly Arg Leu His Lys Thr Glu Asp Gly Gly Trp Glu Trp Ser Asp Asp Glu Phe Asp Glu Glu Ser Glu Glu Gly Lys Ala Ala Ile Ser Gln Leu Arg Ser Pro Arg Val Lys Glu Ser Ile Ser Asn Ser Glu Leu Phe Pro Thr Thr Asp Pro Val Gly Thr Leu Leu Gln Val Pro Glu Gln Ile Ser Ala His Leu Pro Gln Pro Ala Gly Gln Ile Ala Thr Gln Pro Thr Gln Val Ser Leu Pro Pro Thr Ala Glu Pro Ala Lys Thr Ala Gln Ala Leu Ser Ser Gly Ser Gly Ser Gln Glu Thr Lys Ile Pro Ile Ser Leu Val Leu Arg Leu Arg Asn Ser Lys Lys Glu Leu Asn 

Asp Ile Arg Phe Glu Phe Thr Pro Gly Arg Asp Thr Ala Glu Gly Val 450 460

Ser Gln Glu Leu Ile Ser Ala Gly Leu Val Asp Gly Arg Asp Leu Val 465 470 475 480

Ile Val Ala Ala Asn Leu Gln Lys Ile Val Glu Glu Pro Gln Ser Asn 485 490 495

Arg Ser Val Thr Phe Lys Leu Ala Ser Gly Val Glu Gly Ser Asp Ile 500 505 510

Pro Asp Asp Gly Lys Leu Ile Gly Phe Ala Gln Leu Ser Ile Ser 515 520 525

<210> 58

<211> 560

<212> PRT

<213> Saccharomyces cerevisiae

<400> 58

Met Val Leu Leu Lys Glu Pro Val Gln Pro Leu Pro Arg Ser Ser Leu 1 5 10 15

Leu Tyr Asn Asn Ala Ser Asn Ser Ser Ser Arg Ile Lys Glu Thr Arg
20 25 30

Lys Val Lys Leu Leu Tyr Asn Pro Leu Thr Lys Arg Gln Ile Leu Asn 35 40 45

Asn Phe Glu Ile Leu Ala Thr Leu Gly Asn Gly Gln Tyr Gly Lys Val 50 60

Lys Leu Ala Arg Asp Leu Gly Thr Gly Ala Leu Val Ala Ile Lys Ile 65 70 75 80

Leu Asn Arg Phe Glu Lys Arg Ser Gly Tyr Ser Leu Gln Leu Lys Val 85 90 95

Glu Asn Pro Arg Val Asn Gln Glu Ile Glu Val Met Lys Arg Cys His  $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$ 

His Glu Asn Val Val Glu Leu Tyr Glu Ile Leu Asn Asp Pro Glu Ser

Thr	Lys 130	Val	Tyr	Leu	Val	Leu 135	Glu	Tyr	Cys	Ser	Arg 140	Gly	Pro	Val	Lys
Trp 145	Cys	Pro	Glu	Asn	Lys 150	Met	Glu	Ile	Lys	Ala 155	Val	Gly	Pro	Ser	Ile 160
Leu	Thr	Phe	Gln	Gln 165	Ser	Arg	Lys	Val	Val 170	Leu	Asp	Val	Val	Ser 175	Gly
Leu	Glu	Tyr	Leu 180	His	Ser	Gln	Gly	Ile 185	Thr	His	Arg	Asp	Ile 190	Lys	Pro
Ser	Asn	Leu 195	Leu	Ile	Ser	Ser	Asn 200	Gly	Thr	Val	Lys	Ile 205	Ser	Asp	Phe
Gly	Val 210	Ala	Met	Ser	Thr	Ala 215	Thr	Gly	Ser	Thr	Asn 220	Ile	Gln	Ser	Ser
His 225	Glu	Gln	Leu	Leu	Lys 230	Ser	Arg	Ala	Leu	Gly 235	Thr	Pro	Ala	Phe	Phe 240
Ala	Pro	Glu	Leu	Cys 245	Ser	Thr	Glu	Lys	Glu 250	Tyr	Ser	Cys	Ser	Ser 255	Ala
Ile	Asp	Ile	Trp 260	Ser	Leu	Gly	Val	Thr 265	Ile	Tyr	Cys	Leu	Leu 270	Phe	Gly
Lys	Leu	Pro 275	Phe	Asn	Ala	Asn	Ser 280	Gly	Leu	Glu	Leu	Phe 285	Asp	Ser	Ile
Ile	Asn 290	Lys	Pro	Leu	Glu	Phe 295	Pro	Ser	Tyr	Glu	Glu 300	Met	Leu	Asn	Gly
Ala 305	Thr	Ser	Gly	Ile	Thr 310	Met	Glu	Glu	Tyr	Thr 315	Asp	Ala	Lys	Asp	Leu 320
Leu	Lys	Lys	Leu	Leu 325	Gln	Lys	Asp	Pro	Asp 330	Lys	Arg	Ile	Lys	Leu 335	Ala
Asp	Ile	Lys	Val 340	His	Pro	Phe	Met	Cys 345	His	Tyr	Gļy	Lys	Ser 350	Asp	Ala

Ala Ser Val Leu Thr Asn Leu Glu Thr Phe His Glu Leu Lys Val Ser 355 360 365

Pro Pro Ser Ser Cys Lys Arg Val Glu Leu Val Ser Leu Pro Val Asn 370 375 380

Ser Ser Phe Ala Ser Leu Asp Ser Val Tyr Met Glu Asn Phe Asp His 385 390 395 400

Asn Asn Leu Arg Thr Gly Ala Asp Arg Asn Ser Thr Tyr Ser Pro Ser 405 410 415

Ile Tyr Asp Ala Asn Thr Leu Ser Pro Ser Ala Tyr His Asn Ile Gly 420 425 430

Ser Arg Glu Ser Ser Tyr Ser Ser Phe Ser Ser Phe Thr Ser Ser Thr 435

Ala Phe Ala Ser Gln Ile Ser Ile Gln Asp Ala Pro Ala Ile Gly Asp 450 460

Gln Gln Cys Leu Ile Gly Glu Ser Gly Ser Ser Leu Arg Val Asn Ser 465 475 480

Cys Glu Phe Pro Gln Tyr Thr Thr Met Ser Pro Val Gly Glu Tyr Pro  $485 \hspace{1cm} 490 \hspace{1cm} 495 \hspace{1cm}$ 

Phe Glu Ser Thr Glu Ala Ser Leu Ser Ser Thr Leu Thr Pro Val Gly 500 505 510

Asn Val Pro Gln Arg Ile Lys Ala His Leu Val Glu Gly Lys Ser Asn 515 520 525

Ser Lys Asp Asp Leu Arg Ile Glu Ala Asp Ala Ser Leu Val Phe Glu 530 535 540

Ala Ser Asp Ala Gln Arg Thr Arg Arg Met Ser Leu Tyr Lys Leu 545 550 555 560

<210> 59 <211> 1142 <212> PRT <213> Saccharomyces cerevisiae

<400> 59

Met Asp Arg Ser Asp Lys Lys Val Asn Val Glu Glu Val Asn Val Pro 1 5 10 15

Ser Asn Leu Gln Ile Glu Leu Glu Lys Ser Gly Thr Ser Ser Val $20 \\ 25 \\ 30$ 

Ser Leu Arg Ser Pro Thr Lys Ser Ser Ala Thr Asn Leu Ala Gly Met  $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$ 

Ala Glu Gly Ala Arg Asp Asn Ala Ser Ile Ala Ser Ser Ser Val Asp 50 55 60

Ser Leu Asn Met Leu Leu Glu Arg Gln Arg Val Arg Gln Leu Asn His 65 70 75 80

Pro Gln His Gln Gln His Ile Ser Ser Leu Ala Lys Thr Pro Thr 85 90 95

Thr Thr Ser Ser Phe Cys Ser Ser Gly Ser Ser Lys Asn Lys Val Lys 100 105 110

Glu Thr Asn Arg Ile Ser Leu Thr Tyr Asp Pro Val Ser Lys Arg Lys 115 120 125

Val Leu Asn Thr Tyr Glu Ile Ile Lys Glu Leu Gly His Gly Gln His 130 135 140

Gly Lys Val Lys Leu Ala Arg Asp Ile Leu Ser Lys Gln Leu Val Ala 145 150 155 160

Ile Lys Ile Val Asp Arg His Glu Lys Lys Gln Arg Lys Phe Phe Thr \$165\$ \$170\$ \$175\$

Phe Ile Lys Ser Ser Lys Ile Ser Glu Asn Asp Lys Ile Lys Arg Glu 180 185 190

Ile Ala Ile Met Lys Lys Cys His His Lys His Val Val Gln Leu Ile 195 200 205

Glu Val Leu Asp Asp Leu Lys Ser Arg Lys Ile Tyr Leu Val Leu Glu

Tyr 225	Cys	Ser	Arg	Gly	Glu 230	Val	Lys	Trp	Cys	Pro 235	Pro	Asp	Cys	Met	Glu 240
Ser	Asp	Ala	Lys	Gly 245	Pro	Ser	Leu	Leu	Ser 250	Phe	Gln	Glu	Thr	Arg 255	Glu
Ile	Leu	Arg	Gly 260	Val	Val	Leu	Gly	Leu 265	Glu	Tyr	Leu	His	Tyr 270	Gln	Gly
Ile	Ile	His 275	Arg	Asp	Ile	Lys	Pro 280	Ala	Asn	Leu	Leu	Ile 285	Ser	Gly	Asp
Gly	Thr 290	Val	Lys	Ile	Ser	Asp 295	Phe	Gly	Val	Ser	Leu 300	Ala	Ala	Ser	Ser
Thr 305	Asn	Ser	Ser	Asp	Ser 310	Ser	Glu	Ser	Leu	Asp 315	Glu	Leu	Glu	Leu	Ala 320
Lys	Thr	Val	Gly	Thr 325	Pro	Ala	Phe	Phe	Ala 330	Pro	Glu	Met	Cys	Leu 335	Gly
Glu	Asp	Ala	Phe 340	Thr	Arg	Tyr	Asn	Leu 345	Thr	Lys	Glu	Asn	Leu 350	Phe	Arg
Gly	Ser	Cys 355	Ile	Ser	Phe	Met	Ile 360	Asp	Ile	Trp	Ala	Val 365	Gly	Val	Thr
Leu ,	Tyr 370	Cys	Leu	Leu	Phe	Gly 375	Met	Leu	Pro	Phe	Phe 380		Asp	Phe	Glu
Leu 385	Lys	Leu	Phe	Glu	Lys 390	Ile	Val	Asn	Asp	Pro 395	Leu	Lys	Phe	Pro	Thr 400
Phe	Lys	Glu	Ile	Gln 405	Ser	Asn	Lys	Val	Ser 410	Lys	Val	Ser	Cys	Glu 415	Glu
Glu	Tyr	Glu	Met 420	Ala	Lys	Asp	Leu	Leu 425	Leu	Lys	Leu	Leu	Glu 430	Lys	Asn
Pro	Gln	Lys 435	Arg	Met	Thr	Ile	Pro 440	Ala	Ile	Lys	Lys	His 445	Pro	Phe	Val

Ser Val Leu Glu Gln Lys Leu Arg Phe Gln Cys Asn Gln Thr Asp Gln 470 475 Phe Glu Pro Ile Ser Ile Ser Lys His Glu Leu Lys Asn Ala Val Ser Gly Val Gly Lys Lys Ile Lys Glu Ser Val Leu Lys Ser Ile Pro Leu Lys Asp Pro Ser Asp Leu Ser Asn Lys Asn Tyr Leu His Pro Thr Glu Thr Thr Arg Gly Arg Gly Asp Ala Asn Val Ile Val Ser Glu Gly Ser Val Leu Ser Asn Ile Lys Glu Leu Ser Ala Asn Asp Gly Cys Leu Asn Thr Asp Ser Asp Thr Asn Ile Asn Ile Asn Asp Asp Asp His Tyr Ser Gly Asp Asp Asn Asp Gly His Leu Thr Lys Arg Glu Leu Glu Arg Glu Leu Asn Lys Phe Asp Asp Lys His Glu Ala Gly Asn Met Val Asn Leu Pro Ile Asn Ser Ser Phe Ala Ser Leu Asp Ser Phe Tyr Ile Asp Asn Phe Ala Met Ala Arg Met Gly Met Ser Ser Pro Glu Ala Gly Asp Ser Val Ser Ser Val Pro Asn Leu Pro Ser Ala Pro Ser Ser Thr Arg Leu Gly Arg Ser Pro Val Phe Ser Gly Val Thr Asn Gln Pro Ser Pro Ile 

Ser Trp Asp Phe Asp His Val Pro Glu Asn Asp Glu Lys Leu Leu Ser

675 680 Tyr Asp Lys Ser His Asn Ser Leu Leu Arg Asn Ser Ser His Leu 700 690 695 Thr Ser Tyr Asn Ser Gly Arg Pro Ser Ser Arg Thr Gly Arg Met Asn 710 715 Ser Arg Asn Gln Asn Leu Pro Lys Ile Pro Asn Ser Leu Ser Lys Ile 730 Ser Thr Thr Lys Leu Thr Glu Leu Arg Val Pro Lys Asp Ser Glu Ile Pro Ser Pro Ala Lys Asn Pro Asn Ala Asp Arg Leu Arg Arg Phe Pro 760 Val Lys Lys Asn Thr Lys Thr Pro Ala Ile Lys Asp Pro Pro Arg Ile Asn Ile Asn Ser Ser Asp Lys Ser Gly Ser Lys Asn Ser Pro Ile Lys Ser Leu Tyr Gln Arg Met Lys Gln Ser Lys Asp Asn Ser Lys Thr Phe 810 Glu Val Arg Arg Gly Asn Phe Phe Ser His Phe Asn Gly Asp Asp Asp 820 825 830 Asp Ser Ser Ser Gln Ser Ser Val Thr Ser Ser Gly Ser Glu Ser Asp 835 840 Ser Glu Leu Ser Ser Thr Ser Ser Ser Cys Thr Ser Gly Thr Gln Ser 855 Arg Asn Ser Ser Asn Asn Ala Tyr Ser Glu Thr Glu Ser Leu Pro 865 870 875 Phe Glu Phe Gly Val Asp Ser Glu Asp Gly Ser Gly Val Leu Leu Arg

890

885

Arg Pro Val Leu Pro Gln Gln Lys Ser Ser Phe Cys Ala Thr Gly Arg

- Asp Leu Pro Asn Glu Asp Gln Ile Arg Pro Phe Leu Asp Ile Gln Pro 900 905 910
- Cys Arg Met Lys Val Lys Ser Ser Leu Asn Leu Glu Pro Pro Ser 915 920 925
- Val Ser Ser Ser Ser Ser Ser Ser Asp Glu Asp Glu Leu Ile Leu 930 935 940
- Asn Val Gly Thr Ala Gly His Arg Arg His Asn Ser Ser Lys Leu 945 950 955 960
- Ser Glu Leu Ser Asn Ser Pro Gln Lys Gly Ser Asn Asn Phe Met Tyr 965 970 975
- Ser Asn Gly Ser Val His Asp Ser Glu Thr Thr Ile Thr Pro Gln Asn 980 985 990
- Met Asp Asp Leu Thr Leu His Gln Ala Leu Ser Arg Ser Gln Pro Ile 995 1000 1005
- Ser Lys Pro Gly Pro Leu Val Leu Pro Lys Arg Leu Asp Gln Lys 1010 1015 1020
- Lys Ala Thr Thr Glu Thr Ser Asn Leu Thr Asp Ile Val Glu Phe 1025 1030 1035
- Asn Gly Asn Asn Asp His Arg Lys Asp Lys Asn Phe Asp Lys Val 1040 1045 1050
- Leu Tyr Ser Arg Asp Leu Leu Lys Asp Ala Leu Ser Ser Thr Asn 1055 1060 1065
- Ala Gly Arg Arg Arg Ser Ile Pro Ser Asn Lys Ile Arg Gly Arg 1070 1075 1080
- Lys Asp Ala Ser Ile Thr Met Ser Thr Asn Val Gly Asn Asp Glu 1085 1090 1095
- His Ala Arg Asn Thr Ser Cys His Gly Asp Lys Gly Gln Glu Asn 1100 1105 1110
- Gly Ala Ile Lys Gln Arg Thr His Glu Arg Ser Arg Ser Leu Thr

1115 1120 1125

Val Ala Glu Leu Asn Glu Glu Lys Arg Arg Ser Ala Leu Pro 1130 1135 1140

<210> 60

<211> 640

<212> PRT

<213> Saccharomyces cerevisiae

<400> 60

Leu Ser Gln Gln Ser Cys Ile Arg Glu Asp Glu Leu Asp Ser Pro Pro 20 25 30

Ile Thr Pro Thr Ser Gln Thr Ser Ser Phe Gly Ser Ser Phe Ser Gln 35 40 45

Gln Lys Pro Thr Tyr Ser Thr Ile Ile Gly Glu Asn Ile His Thr Ile 50 60

Leu Asp Glu Ile Arg Pro Tyr Val Lys Lys Ile Thr Val Ser Asp Gln 65 70 75 80

Asp Lys Lys Thr Ile Asn Gln Tyr Thr Leu Gly Val Ser Ala Gly Ser 85 90 95

Val Val Ala Val Lys Ile Ile Pro Lys Lys Pro Trp Asn Ala Gln Gln 115 120 125

Tyr Ser Val Asn Gln Val Met Arg Gln Ile Gln Leu Trp Lys Ser Lys 130 135 140

Gly Lys Ile Thr Thr Asn Met Ser Gly Asn Glu Ala Met Arg Leu Met 145 150 155 160

Asn Ile Glu Lys Cys Arg Trp Glu Ile Phe Ala Ala Ser Arg Leu Arg 165 170 175

Ser Glu Ser Ile Trp Ile Val Thr Asn Trp Cys Ser Leu Gly Glu Leu Gln Trp Lys Arg Asp Asp Glu Asp Ile Leu Pro Gln Trp Lys Lys Ile Val Ile Ser Asn Cys. Ser Val Ser Thr Phe Ala Lys Lys Ile Leu Glu Asp Met Thr Lys Gly Leu Glu Tyr Leu His Ser Gln Gly Cys Ile His Arg Asp Ile Lys Pro Ser Asn Ile Leu Leu Asp Glu Glu Lys Val Ala Lys Leu Ser Asp Phe Gly Ser Cys Ile Phe Thr Pro Gln Ser Leu Pro Phe Ser Asp Ala Asn Phe Glu Asp Cys Phe Gln Arg Glu Leu Asn Lys Ile Val Gly Thr Pro Ala Phe Ile Ala Pro Glu Leu Cys His Leu Gly Asn Ser Lys Arg Asp Phe Val Thr Asp Gly Phe Lys Leu Asp Ile Trp Ser Leu Gly Val Thr Leu Tyr Cys Leu Leu Tyr Asn Glu Leu Pro Phe Phe Gly Glu Asn Glu Phe Glu Thr Tyr His Lys Ile Ile Glu Val Ser Leu Ser Ser Lys Ile Asn Gly Asn Thr Leu Asn Asp Leu Val Ile Lys Arg Leu Leu Glu Lys Asp Val Thr Leu Arg Ile Ser Ile Gln

Asn Asn Val His Ile Val Arg Leu Ile Glu Cys Leu Asp Ser Pro Phe

Asp Leu Val Lys Val Leu Ser Arg Asp Gln Pro Ile Asp Ser Arg Asn 405 410 415

His Ser Gln Ile Ser Ser Ser Ser Val Asn Pro Val Arg Asn Glu Gly 420 425 430

Pro Val Arg Arg Phe Phe Gly Arg Leu Leu Thr Lys Lys Gly Lys Lys 435 440 445

Lys Thr Ser Gly Lys Gly Lys Asp Lys Val Leu Val Ser Ala Thr Ser 450 455 460

Lys Val Thr Pro Ser Ile His Ile Asp Glu Glu Pro Asp Lys Glu Cys 465 470 475 480

Phe Ser Thr Thr Val Leu Arg Ser Ser Pro Asp Ser Ser Asp Tyr Cys 485 490 495

Ser Ser Leu Gly Glu Glu Ala Ile Gln Val Thr Asp Phe Leu Asp Thr 500 505 510

Phe Cys Arg Ser Asn Glu Ser Leu Pro Asn Leu Thr Val Asn Asn Asp 515 520 525

Lys Gln Asn Ser Asp Met Lys Thr Asp Arg Ser Glu Ser Ser His 530 540

Ser Ser Leu Lys Ile Pro Thr Pro Ile Lys Ala Met Ile Arg Leu Lys 545 550 555 560

Ser Ser Pro Lys Glu Asn Gly Asn Arg Thr His Ile Asn Cys Ser Gln 565 570 575

Asp Lys Pro Ser Ser Pro Leu Met Asp Arg Thr Val Gly Lys Arg Thr 580 590

Val Asn Asn Ser Gly Ala Arg Lys Leu Ala His Ser Ser Asn Ile Leu 595 600 605

Asn Phe Lys Ala Tyr Ile Asn Ser Glu Asp Ser Asp Ile Arg Glu Thr 610 620

Val Glu Asp Val Lys Thr Tyr Leu Asn Phe Ala Asp Asn Gly Gln Ile

625		630	635	640
<210>	61			

<211> 545 <212> PRT <213> Homo sapiens

<400> 61

Met Ser Ser Cys Val Ser Ser Gln Pro Ser Ser Asn Arg Ala Ala Pro

Gln Asp Glu Leu Gly Gly Arg Gly Ser Ser Ser Glu Ser Gln Lys

Pro Cys Glu Ala Leu Arg Gly Leu Ser Ser Leu Ser Ile His Leu Gly

Met Glu Ser Phe Ile Val Val Thr Glu Cys Glu Pro Gly Cys Ala Val

Asp Leu Gly Leu Ala Arg Asp Arg Pro Leu Glu Ala Asp Gly Gln Glu 70

Val Pro Leu Asp Thr Ser Gly Ser Gln Ala Arg Pro His Leu Ser Gly

Arg Lys Leu Ser Leu Gln Glu Arg Ser Gln Gly Gly Leu Ala Ala Gly 100 105

Gly Ser Leu Asp Met Asn Gly Arg Cys Ile Cys Pro Ser Leu Pro Tyr 115 120

Ser Pro Val Ser Ser Pro Gln Ser Ser Pro Arg Leu Pro Arg Arg Pro 130 135

Thr Val Glu Ser His His Val Ser Ile Thr Gly Met Gln Asp Cys Val 150 155 .145

Gln Leu Asn Gln Tyr Thr Leu Lys Asp Glu Ile Gly Lys Gly Ser Tyr 165

Gly Val Val Lys Leu Ala Tyr Asn Glu Asn Asp Asn Thr Tyr Tyr Ala 185 180

Arg Arg Pro Pro Pro Arg Gly Thr Arg Pro Ala Pro Gly Gly Cys Ile 210 220 Gln Pro Arg Gly Pro Ile Glu Gln Val Tyr Gln Glu Ile Ala Ile Leu 225 230 235 Lys Lyu Leu Asp His Pro Asn Val Val Lys Leu Val Glu Val Leu Asp 245 250 Asp Pro Asn Glu Asp His Leu Tyr Met Val Phe Glu Leu Val Asn Gln 265 Gly Pro Val Met Glu Val Pro Thr Leu Lys Pro Leu Ser Glu Asp Gln 280 Ala Arg Phe Tyr Phe Gln Asp Leu Ile Lys Gly Ile Glu Tyr Leu His 295 Tyr Gln Lys Ile Ile His Arg Asp Ile Lys Pro Ser Asn Leu Leu Val 305 310 315 Gly Glu Asp Gly His Ile Lys Ile Ala Asp Phe Gly Val Ser Asn Glu 325 330

Met Lys Val Leu Ser Lys Lys Leu Ile Arg Gln Ala Gly Phe Pro

200

195

Phe Lys Gly Ser Asp Ala Leu Leu Ser Asn Thr Val Gly Thr Pro Ala 340 345 350

Phe Met Ala Pro Glu Ser Leu Ser Glu Thr Arg Lys Ile Phe Ser Gly 355 360 365

Lys Ala Leu Asp Val Trp Ala Met Gly Val Thr Leu Tyr Cys Phe Val 370 375 380

Phe Gly Gln Cys Pro Phe Met Asp Glu Arg Ile Met Cys Leu His Ser 385 390 395 400

Lys Ile Lys Ser Gln Ala Leu Glu Phe Pro Asp Gln Pro Asp Ile Ala 405 410 415

Glu Asp Leu Lys Asp Leu Ile Thr Arg Met Leu Asp Lys Asn Pro Glu 420 425 430

Ser Arg Ile Val Val Pro Glu Ile Lys Ile Leu Val Lys Thr Met Ile 435 440 445

Arg Lys Arg Ser Phe Gly Asn Pro Phe Glu Gly Ser Arg Arg Glu Glu 450 455 460

Arg Ser Leu Ser Ala Pro Gly Asn Leu Leu Thr Lys Lys Pro Thr Arg 465 470 475 480

Glu Cys Glu Ser Leu Ser Glu Leu Lys Glu Ala Arg Gln Arg Arg Gln 485 490 495

Pro Pro Gly His Arg Pro Ala Pro Arg Gly Gly Gly Ser Ala Leu 500 505 510

Val Arg Gly Ser Pro Cys Val Glu Ser Cys Trp Ala Pro Ala Pro Gly 515 520 525

Ser Pro Ala Arg Met His Pro Leu Arg Pro Glu Glu Ala Met Glu Pro 530 540

Glu 545

<210> 62 <211> 243

<211> 243 <212> PRT

<213> Artificial

<220>

<223> Consensus for figure 12

<400> 62

Pro Ser Ser Ser Ser Ser Arg Ile Lys Thr Val Leu Tyr Pro Leu 1 5 10 15

Thr Lýs Arg Gln Ile Leu Asn Asn Tyr Ile Leu Gly Gly Gln Tyr Gly 20 25 30

Lys Val Lys Leu Ala Asp Thr Leu Val Ala Ile Lys Ile Leu Lys Lys 35 40 45

Lys Lys Tyr Lys Asp Arg Val Lys Glu Ile Val Met Lys Arg Leu His 50

His Asn Val Val Leu Ile Glu Val Leu Asp Asp Pro Ser Lys Val Tyr 65

Leu Val Leu Glu Tyr Cys Ser Gly Val Trp Cys Met Glu Ile Val Pro 85 90 . 95

Ile Leu Ser Gln Ala Arg Val Val Asp Val Val Gly Leu Glu Tyr Leu 100 105 110

His Ser Gln Gly Ile Ile His Arg Asp Ile Lys Pro Ser Asn Ile Leu 115 120 125

Ile Ser Asp Gly Thr Val Lys Ile Ser Asp Phe Gly Val Thr Ser Asp 130 135 140

Ser Leu Arg Val Gly Thr Pro Ala Phe Ala Pro Glu Leu Cys Tyr Phe 145 150 155 160

Ile Asp Ile Trp Ser Leu Gly Val Thr Leu Tyr Cys Leu Leu Phe Gly 165 170 175

Leu Pro Phe Ala Asp Leu Leu Phe Asp Lys Ile Ile Leu Phe Pro Glu 180 185 190

Met Glu Glu Leu Lys Asp Leu Leu Lys Lys Leu Leu Glu As<br/>n Lys Asn 195 200 205

Pro Lys Arg Ile Leu Ile Lys His Pro Phe Val Asp His Pro Asp Val 210 215 220

Leu Thr Glu Leu Lys Pro Leu Arg Val Glu Pro Val Ser Leu Lys Ser 225 230 235 240

Ser Leu Gly

<210> 63

<211> 25

<212> PRT

<213> Homo sapiens

<400> 63

Gly Thr Pro Glu Tyr Leu Ala Pro Glu 20 25

<210> 64

<211> 28

<212> PRT

<213> Homo sapiens

<400> 64

Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu 20 25

<210> 65

<211> 27

<212> PRT

<213> Homo sapiens

<400> 65

Asp Phe Gly Leu Ser Asn Leu Tyr Gln Lys Asp Lys Phe Leu Gln Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Phe Cys Gly Ser Pro Leu Tyr Ala Ser Pro Glu 20 25

<210> 66

<211> 26

<212> PRT

<213> Homo sapiens

<400> 66

Asp Phe Gly Leu Ser Asn Tyr His Gln Gly Lys Phe Leu Gln Thr Phe 1 5 10 15

Cys Gly Ser Pro Leu Tyr Ala Ser Pro Glu

<210> 67

```
<211> 27
<212> PRT
<213> Homo sapiens
<400> 67
Asp Phe Gly Met Ala Ser Leu Gln Val Gly Asp Ser Leu Leu Glu Thr
                                     10
Ser Cys Gly Ser Pro His Tyr Ala Cys Pro Glu
        20
<210> 68
<211> 27
<212> PRT
<213> Homo sapiens
<400> 68
Asp Phe Gly Met Ala Ser Leu Gln Val Gly Asp Ser Leu Leu Glu Thr
Ser Cys Gly Ser Pro His Tyr Ala Cys Pro Glu
            20
<210> 69
<211> 27
<212> PRT
<213> Homo sapiens
<400> 69
Asp Phe Gly Phe Gly Asn Phe Tyr Lys Ser Gly Glu Pro Leu Ser Thr
                5
                                     10
Trp Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu
            20
                                 25
<210> 70
<211> 27
<212> PRT
<213> Homo sapiens
<400> 70
Asp Phe Gly Phe Gly Asn Phe Phe Lys Ser Gly Glu Leu Leu Ala Thr
Trp Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu
```

20

```
<210> 71
<211> 27
<212> PRT
<213> Arabidopsis thaliana
<400> 71
Asp Phe Gly Leu Ser Asn Ile Met Arg Asp Gly His Phe Leu Lys Thr
                                     10
Ser Cys Gly Ser Pro Asn Tyr Ala Ala Pro Glu
<210> 72
<211> 27
<212> PRT
<213> Arabidopsis thaliana
<400> 72
Asp Phe Gly Leu Ser Asn Val Met Arg Asp Gly His Phe Leu Lys Thr
                                     10
Ser Cys Gly Ser Pro Asn Tyr Ala Ala Pro Glu
            20
<210> 73
<211>
       27
<212>
       PRT
<213> Homo sapiens
<400> 73
Asp Phe Gly Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr
                                     10
Ser Cys Gly Ser Pro Asn Tyr Ala Ala Pro Glu
            20
<210> 74
<211> 27
<212>
      PRT
<213> Homo sapiens
<400> 74
Asp Phe Gly Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr
```

```
Ser Cys Gly Ser Pro Asn Tyr Ala Ala Pro Glu
<210> 75
       27
<211>
<212> PRT
<213> Saccharomyces cerevisiae
<400> 75
Asp Phe Gly Leu Ser Asn Ile Met Thr Asp Gly Asn Phe Leu Lys Thr
Ser Cys Gly Ser Pro Asn Tyr Ala Ala Pro Glu
<210> 76
<211> 27
<212> PRT
<213> Homo sapiens
<400> 76
Asp Phe Gly Phe Ser Asn Leu Phe Thr Pro Gly Gln Leu Leu Lys Thr
                                    10
Trp Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu
<210> 77
<211> 29
<212> PRT
<213> Homo sapiens
<400> 77
Asp Phe Gly Leu Cys Ala Lys Pro Lys Gly Asn Lys Asp Tyr His Leu
                                    10
Gln Thr Cys Cys Gly Ser Leu Ala Tyr Ala Ala Pro Glu
                                25
<210> 78
<211> 21
<212> PRT
<213> Artificial
<220>
```

<223> consensus from figure 19

<400> 78

Asp Phe Gly Leu Ser Asn Leu Gly Phe Leu Thr Ser Cys Gly Ser Pro 1 5 10 15

Tyr Ala Ala Pro Glu 20

<210> 79

<211> 27

<212> PRT

<213> Homo sapiens

<400> 79

Phe Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu 20 25

<210> 80

<211> 27

<212> PRT

<213> Homo sapiens

<400> 80

Asp Phe Gly Phe Ser Asn Glu Phe Thr Val Gly Asn Lys Leu Asp Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Phe Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu 20 25

<210> 81

<211> 27

<212> PRT

<213> Homo sapiens

<400> 81

Asp Phe Gly Phe Ser Asn Glu Phe Thr Val Gly Gly Lys Leu Asp Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Phe Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu 20 25

<210> 82

```
<211> 27
<212> PRT
<213> Homo sapiens
<400> 82
Asp Phe Gly Phe Ser Asn Glu Phe Thr Leu Gly Ser Lys Leu Asp Thr
Phe Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu
<210> 83
<211> 23
<212> PRT
<213> Homo sapiens
<400> 83
Leu Ser Asn Leu Tyr His Gln Gly Lys Phe Leu Gln Thr Phe Cys Gly
Ser Pro Leu Tyr Arg Arg Arg
            20
<210> 84
<211> 23
<212> PRT
<213> Homo sapiens
<400> 84
Phe Gly Asn Phe Tyr Lys Ser Gly Glu Pro Leu Ser Thr Trp Cys Gly
                5
                                    10
Ser Pro Pro Tyr Arg Arg Arg
            20
<210> 85
<211> 23
<212> PRT
<213> Homo sapiens
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Leu Ser Asn Met Met Ser Asp Gly Glu Phe Leu Arg Thr Ser Cys Gly
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His Gly Ser Tyr Val Thr Lys Arg Gln Ser Thr Lys Leu Leu Ala Ser 245 250 255

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Leu His Tyr Gly Thr Met Phe Arg Glu Cys Ile Arg His Gln Ile Val 145 150 155 160

Ala Lys Tyr Val Leu Asp Ser Glu His Val Lys Lys Phe Phe Tyr Tyr 165 170 175

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